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PSYCHOSOMATIC BACKACHE*

MAJOR MORGAN SARGENT, M.C., A.U.S.†

ALTHOUGH in most discussions of backache there has been a tendency to stress the pathologic conditions that are present,[1] yet the fact that the symptoms may exist without definite disease or deformities is undoubtedly recognized by all who must deal with the problem.[2] In this paper, however, it is desired to suggest that the differential diagnosis of backache is incomplete without the consideration of psychogenic factors, for the latter are important not only as causes but also as contributing factors in cases of organic disease. The symptom of backache, like that of headache, is difficult to evaluate, and at times constitutes a minor form of malingering. Because of its frequency, particularly in military personnel, the symptom is often dismissed after casual and brief examination.

Backache is a relatively frequent complaint among patients suffering from anxiety states. An unusual opportunity has arisen in an Army Air Forces convalescent hospital, in which the primary mission is the treatment of cases of severe anxiety states, to examine large numbers of patients suffering from neurotic symptoms and incidentally complaining of backache.

These patients are for the most part men who have returned from combat tours in all parts of the world, and who on admission are suffering from symptoms of nervousness, insomnia, tension, irritability, restlessness, depression, startle reactions and other neurotic complaints. The causation and treatment of these conditions have been thoroughly described by Grinker and Spiegel.[3] Most of these patients are former members of air crews. A few who are not fliers have had long periods of general duty in distant theaters. Their symptoms have been brought on by long separation from home, privation, loneliness and difficult climatic conditions. No patients have been seen in whom backache was the only complaint.

The patients complaining of backache seen in this hospital fall, with considerable overlapping, into three main groups. In the first group are those in whom definite organic disease is found. It has been the policy when dealing with backache to rule out every possible organic cause by careful clinical examination, x-ray and laboratory studies and, when indicated, additional orthopedic consultation at a nearby Army Air Forces regional station hospital. The proportion of cases in which organic disease alone has been found is less than 4 per cent. The treatment of these cases is primarily an orthopedic problem, and as such has been handled separately from the psychiatric problem. In the second group are the cases with hysterical conversion symptoms. In this classification are included patients of two categories — those suffering from what is considered to be a simple hysterical conversion symptom, and those who have in the past had some evidence of organic disease and at the time of admission appear to be exaggerating their complaints or to have had excessive prolongation of symptoms. Few if any of the patients were thought to have symptoms of a purely hysterical conversion. Practically all those in this group gave a history of some previous injury to the back, often incurred many years previously, and the point of interest is that although many of them had had absolutely no difficulty for many years, they again developed symptoms concomitant with the onset of stress in their Army life.

The following case is illustrative of the way in which the nervous symptoms are held in check by the conversion symptoms. This patient had fallen down some steps twelve years previously, landing on the base of the spine. He believed that this had caused a permanent injury, and said that for the last three or four years he had had an intermittent low backache. On examination he complained of slight pain in the region of the lumbosacral joint on backward bending, but the examination was otherwise negative. X-ray examination of the lumbosacral spine and pelvis showed a small spina bifida occulta of the fifth lumbar vertebra but was otherwise negative. The patient made the interesting and wholly spontaneous statement that when his backache disappeared he experienced extreme anxiety.

Many other patients sustained injuries during combat that were followed by prolonged persistence of symptoms. In a typical case of this kind, the patient complained of backache in the lower dorsal and upper lumbar region, which took the form of

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a dull ache most of the time and was aggravated by exercise and fatigue. On March 18, 1944, he was thrown against a tree by a bomb explosion, was said to have had fractures of the spine and was placed in a body cast for three months. On removal of the cast he was given a back brace, which he wore for the next nine months, although he felt little benefit from it. Since the injury he had been extremely nervous, and he told the examiner that his back bothered him most when he was "nervous." After his return to this country through medical channels, he was kept in various hospitals. Although his back was x-rayed many times, all available reports were completely negative and showed no evidence of old injuries. Examination in this hospital revealed slightly increased prominence of the spinous process of the eighth dorsal vertebra and tenderness over the spinous processes of the lower dorsal and upper lumbar vertebras. There was considerable spasm of the paravertebral muscles, particularly on the right. Motions of the back were entirely normal. Treatment consisted of psychotherapy and exercises for the back, and the brace was discarded. The back symptoms improved somewhat, but the patient was eventually discharged from the Army on the basis of a severe anxiety reaction. His nervous symptoms had begun at the time of injury. It was impossible to find out what had happened to the patient's back at the time of the blast, since the accident occurred at an outlying base in the jungle and no records were sent with the patient. One can only surmise from the x-ray reports taken after removal of the cast either that there had been no actual fractures or that, if present, they were not too severe and healed without residual evidence. This patient was treated as a physical invalid for a year, during which time he tended to exhibit exaggerated symptoms. He also showed symptoms of backache due to muscular tension.

Another patient showing conversion symptoms was injured in a crash landing in July, 1944, being struck in the lower back by a piece of metal, which caused a contusion. After having his back strapped by his flight surgeon, he continued flying. In the following month, he was shot down, captured and interned in a neutral country, where he received no specific treatment. Since that time he had had a dull ache in the lower back, which after long standing or sitting extended up the paravertebral muscles. Examination at this hospital revealed diffuse and moderate tenderness in the lumbosacral area and over the lower sacrospinalis muscle groups, with moderate spasm of the muscles of the lower back. X-ray examination of the spine and pelvis showed slight roughening of the apophyseal articulations of the fifth lumbar and first sacral vertebras, particularly on the left. Because of these findings, physiotherapy was given in the form of baking with infra-red rays and massage, but with no relief of symptoms. Approximately one month after entering the hospital, the patient developed symptoms of acute appendicitis, and appendectomy was performed under spinal anesthesia. Throughout the operation the patient complained of pain in the lumbosacral area, and at its conclusion this complaint was investigated. The anesthesia, which had been completely satisfactory throughout the operation, was complete at least as high as the ninth dorsal vertebra, but the patient said that he still had an aching pain in the region of the lumbosacral joint. This was obviously impossible on a somatic basis. The symptoms exhibited were considered out of proportion to the extent of the injury, but the x-ray findings, although somewhat questionable, led us to give him the benefit of the doubt, and for several weeks it was believed that he had good reason for the discomfort. Incidentally, the backache improved considerably during the course of psychotherapeutic interviews.

Even superficial psychiatric examinations revealed that the patients whose backache was thought to be mostly a conversion symptom showed comparatively fewer symptoms of overt anxiety and nervousness. Practically all the patients in this group were enlisted men, and taken collectively they appeared to be somewhat less anxious than their associates. The fact that they were enlisted men is significant only in that the level of education of the group as a whole is lower than that of the officers.

By far the largest number of patients with backache fall into the third group of cases, which are considered functional in type, the backache being due to muscular tension, the somatic manifestation of increased nervous tension. These patients exhibited all the symptoms associated with operational fatigue. As a rule they were tense and nervous, complained of insomnia and combat dreams, and found it difficult to sit still for any length of time. The more restless they were, the severer the backache was. Most of them complained of aching pain in the lower lumbar or lumbosacral region, but others located their pain in the lower dorsal area and a few described it as in the upper dorsal or posterior cervical area. The backache is usually intermittent. The pain may not be felt for hours or even days, and it is most frequently complained of at night, early in the morning and after exercise or long standing or sitting. Although in the less acute cases an increase in muscular tension is not always demonstrable, in the severer cases it can be easily elicited by palpation, particularly in the sacrospinalis and erector spinae muscle groups, and at times the muscles go into almost boardlike spasms. Several patients have been seen in whom the back muscles were under such tension, even in a relaxed position, that fibrillary contractions were visible. These patients exhibit signs and symptoms of easy muscular fatigue, which is easily

noticeable among the severe cases and is partly proved by the poor showings made during tests of physical fitness. Consequently, it is believed that increased tension of muscles that are easily fatigued tends to cause symptoms far more easily than it does in more normal muscles. When demonstrable tension is present by palpation, there is often some limitation of forward bending, with an increase in pain, and there is some pain on straight leg raising and also on forward tilting of the pelvis with both flexed knees brought up toward the chest.

The signs and symptoms often vary in the same patient from day to day, as one would expect when the muscular tension is the result of nervous tension. Many of these patients have considerable difficulty in sleeping, and when once asleep they have combat and anxiety dreams that keep them tense and restless throughout the night. This is apparently the reason why so many patients complain of backache during the night and on awakening in the morning. The inability of the muscles to secure rest results in a constant state of fatigue, and it is small wonder that any additional burden placed on them by exercise or by long use in the maintenance of posture results in protest, which is manifested by pain and aches.

In contrast with the patients suffering from backache due to organic causes and with those with conversion symptoms, almost all patients with backache due to muscular tension complain of a rather diffuse ache, which they can localize only in the general region of the back. A large number of these patients attribute the onset of symptoms to some injury, but as a rule the injury is known not to have been severe, and at times evidence of it is almost nonexistent. This is illustrated by a patient who first noticed low lumbar backache in October, 1944, which developed after a burst of flak beneath the ball turret in which he was riding. At that time he was not injured, either by the flak or by concussion. On his admission to this hospital five months later, after completion of his combat tour, he complained of low lumbar backache, usually coming on in the morning, wearing off during the day and coming on again toward the evening. Examination of the back revealed an extreme degree of tension in the sacrospinalis muscle groups. X-ray examination of the lumbosacral spine was negative, and at the time of examination it was thought that the backache was a purely psychosomatic symptom due to muscular tension.

Another patient stated that off and on for fifteen years he had suffered low-back pain, which came on at times of excitement. He noticed this particularly while flying and when in a tight spot. There was no history of any injury. Examination revealed only marked spasm of both sacrospinalis groups.

Considerable difficulty exists in the correct evaluation of cases when the main problem seems to be muscular tension but careful examination reveals some organic finding that may contribute to the picture. A typical case is that of a patient who suffered an injury to the lower back in December, 1943, when his plane was ditched. After a short period of disability he had little trouble until August, 1944, when he struck his back and strained it severely on falling from a catwalk into the bomb bay of a B-17. Since then he had had lumbar backache, present mostly when exercising. Examination of the back revealed moderate diffuse tenderness in the lumbosacral region and over the lower lumbar muscles. There was no postural deformity, and x-ray films of the spine were negative. Complaints of back pain continued and were greatly aggravated by a train ride while on furlough. It was believed that the patient might have chronic low-back strain but that most of the symptoms were psychosomatic in origin.

Another example of this type of patient is one who complained of low lumbar backache that first came on during his combat mission. There was no history of injury. On several occasions clinical examinations revealed nothing abnormal, but the patient said that his back ached most in the morning and late evening. X-ray examination showed some roughening between the apophyseal articulations of the fourth and fifth lumbar vertebras. This was taken into account, but it was thought that the symptoms were due to muscular tension, which probably aggravated and perhaps made symptomatic the organic disease.

The pain in a great many of these cases is closely similar to that produced by protective muscle spasm in injuries of the lower back. Indeed, it is often of the same type, since it is generally believed that the pain of protective muscle spasm is caused by the persistent pull of muscles on their periosteal attachments. Therefore, in cases in which an injury such as a muscular or ligamentous sprain or strain has occurred within a period of eight to twelve weeks, one cannot say with any degree of certainty that the discomfort is not entirely of organic origin. In our opinion, however, without proved organic disease sufficient to cause it, the prolongation of such pain for several months is generally indicative of muscular tension arising from some other cause, presumably increased nervous tension.

Many cases have been encountered in which backache was undoubtedly due solely to tension, and in most of these cases the pain disappeared after a brief period of psychotherapy for the anxiety state. The discomfort of those with concomitant organic disease is often greatly relieved, but even with the combination of psychotherapy and orthopedic treatment the results are, quite understandably, not entirely satisfactory in all cases.

The treatment of patients with backache due to conversion symptoms or caused by increased muscu-

lar tension must of necessity be primarily psychiatric. In patients with conversion symptoms, it has been found by experience that attempts to deal with the problem by means of physiotherapy, injections of novocain and medical measures tends to focus the patient's attention on the symptom and, if anything, to cause it to become fixed. The same thing is also true, perhaps to a lesser extent, of patients with backache due to muscular tension. Physical and medical procedures are only palliative. Physiotherapy can be carried on for weeks with temporary relief of discomfort for one or two hours after a treatment, or perhaps a little longer, but the symptoms invariably recur. Because of this, we believe that physiotherapy should be reserved for selected cases, usually those with definite organic difficulties, and that it should not be used for cases with conversion or purely tension symptoms. In this hospital the efforts of the Surgical Department to co-operate with the Neuropsychiatric Department have met with considerable success. These results have been accomplished, first, by ruling out the organic difficulties and reassuring the patient that nothing is being overlooked in the attempt to track down the cause of his symptoms, and, second, in preparing the patient for the full benefit of psychotherapy by endeavoring to explain to him in simple terms some of the causes of his backache.

Most of the patients with backache due to muscular tension reveal at some time during their examination the presence of some nervous symptoms, and a little careful questioning leads them to admit that they are more tense than they were previously. In this hospital, where the patients frequently climb upstairs to the various wards, they remark that their legs seem to tire considerably faster than previously or admit to easy muscular fatigue while engaging in exercise. Most of these patients also state that they have noticed an increase in general muscular tension in one form or another and that they find it difficult to relax. When these points have been demonstrated and the patients have perceived that they apply to themselves, it is pointed out to them that increased nervous tension causes increased muscular tension, and that since the muscles under such tension are seldom given a chance to relax as they would normally do, they are in a state of chronic fatigue; consequently, the patients tire much more easily than usual when subjected to additional stress in the form of exercise, or even in the maintenance of posture when merely sitting or standing. Whether this is always the case may be debatable, but at least the point is understood by the lay mind. The fact that combat and anxiety dreams at night also cause much muscular tension is readily understood by those who experience them. With this brief explanation of the mechanisms involved, the patients are told that whereas they can be given temporary relief by such measures as heat and massage, this treatment is only temporary, and that the way to get permanent relief is to be relieved of the basic nervous tension. They are assured that this can be done by co-operation with the psychiatrist. In some patients this type of explanation seems to be sufficient in itself to cause a considerable decrease in symptoms, and in the majority it is believed that the way is paved for beneficial therapy of the primary condition by the psychiatrist.

Summary

Backache is a frequent complaint among persons with anxiety states.

In a hospital where large numbers of men with anxiety states have been seen, the type of backache observed is due in most cases to hysterical conversion symptoms or to functional backache caused by muscular tension and fatigue. The latter type of backache is by far the most frequent one, but the two types are often associated.

Backaches caused by muscular tension and fatigue improve when the anxiety state is relieved by psychiatric treatment.

It is believed that pain of psychogenic origin should receive careful consideration in the differential diagnosis of any case of backache, especially since it may be closely associated with backache caused by organic disease and is often the cause of the prolongation of symptoms.

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THE USE OF PHTHALYLSULFATHIAZOLE (SULFATHALIDINE) IN COLONIC SURGERY*

ROBERT THOMSON, M.D.,† AND ERNEST M. DALAND, M.D.‡

BOSTON

IN 1941, Poth and Knotts[1] introduced succinylsulfathiazole (sulfasuxidine) as an intestinal antiseptic and bacteriostatic agent. It has proved especially valuable as an adjunct to surgery of the large bowel, as well as in the treatment of certain medical conditions. A further improvement was made in this field with the discovery of phthalylsulfathiazole (sulfathalidine§) by Poth and Ross[2] in 1943. This new drug has the advantage of having twice the bacteriostatic activity of succinylsulfathiazole but requiring only half to one third of its dosage. In addition, the drug has not given rise to any toxic reactions such as have occasionally been seen with succinylsulfathiazole. Mattis et al.,[3] in extensive toxicologic studies on the effect of phthalylsulfathiazole in mice, rats and monkeys, reported no toxic manifestations in spite of large doses administered orally every four hours for thirty days. They found extremely low blood concentrations of free and total sulfathiazole, which they attributed to retention in the gastrointestinal tract of all but small amounts of the drug; the small amount that was absorbed was rapidly excreted by the kidneys. Our studies of the blood and urine concentrations of this drug are in agreement with the findings of these investigators. Furthermore, phthalylsulfathiazole is effective in the presence of diarrhea or in patients who are receiving purgatives, whereas the effectiveness of succinylsulfathiazole under these conditions is greatly reduced.

The stools following the use of phthalylsulfathiazole are solid and retain some of their odor, as opposed to the odorless, semifluid movements that occur after the giving of succinylsulfathiazole. The exact mode of action of these drugs is not yet clearly understood. The chemical and bacteriostatic properties of phthalylsulfathiazole have been studied and reported by Poth and Ross.[4]

In this paper we are reporting our experience with the new drug at the Pondville Hospital, where it has been used in connection with surgery of the large bowel. It has been employed in the preoperative preparation of 51 unselected cases over a period of fifteen months. It has also been used in 12 cases of nonspecific gastroenteritis with diarrhea, in which it has apparently been of definite benefit. Our studies of the blood and urine concentrations of this drug are in agreement with the findings of the above investigators.

The type of case in which phthalylsulfathiazole was used is shown in Table 1. In several of the cases the drug was used more than once, when the operation was done in stages. There was no evidence in any case of sensitivity to the preparation.

In Table 2 are shown the types of operation performed. There were 3 cases in the group given routine preoperative doses of phthalylsulfathiazole in which the patients subsequently refused operation or in which it was considered inadvisable. The administration of the drug was stopped on the morning of operation and was not continued postoperatively in all cases except 1, in which a tumor of the rectovaginal septum was removed. The rectum was opened and repaired during operation, and it was decided to continue the drug. Convalescence was uncomplicated.

In cases of resection of a blind loop of bowel or second-stage posterior excision of the rectum, daily preoperative irrigations with a suspension of phthalylsulfathiazole were given. Of the 9 patients who received resection of tumors of the transverse, descending or rectosigmoid colon, 4 had a preliminary or complementary cecostomy, 4 had Miller–Abbott tube decompression, and 1 had neither. In none of these cases was there any serious postoperative distention.

TABLE 1. *Cases in Which Phthalylsulfathiazole Was Employed.*

DIAGNOSIS	NO. OF CASES
Carcinoma of rectum	30
Carcinoma of left colon and rectosigmoid	13
Carcinoma of right colon	4
Carcinoma of transverse colon	1
Tumor of rectovaginal septum	1
Polyposis of large bowel	1
Carcinoma of urinary bladder	1
Total	51

TABLE 2. *Types of Operation Performed.*

OPERATION	NO. OF CASES
Abdominoperineal resection:	
One-stage	12
Two-stage	2
Resection of tumor, transverse and descending colon and rectosigmoid, with primary anastomosis	9
Palliative colostomy	9
Colostomy revision	5
Right colectomy:	
One-stage	3
Two-stage	1
Colostomy or enterostomy closure	2
Ureterointestinal anastomoses	2
Resection of blind loop of bowel	2
Enteroenterostomy	1
Excision of tumor of rectovaginal septum	1
Total	49

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§The material for this study was supplied by Sharp and Dohme, Incorporated, Philadelphia.

Dosage and Preoperative Preparation

The routine procedure has been to place these patients on a low-residue diet and to begin the administration of phthalylsulfathiazole five or six days before operation. Giving the drug for shorter periods of time preoperatively proved unsatisfactory. It has, however, been given in full dosage for as long as fourteen days without any ill effect. The initial dose is 0.05 gm. per kilogram of body weight, or between 2.5 and 4.5 gm. for most patients. Following this, 1 gm. (two tablets) is given every four hours day and night. Enemas are used preoperatively when indicated; strong purgatives are not employed. Whole blood, plasma and amino acid preparations are used as indicated in the correction of anemia and low serum protein. For twenty-four hours before surgery the patient is given only clear liquids by mouth, and routine doses of sulfadiazine are administered during this period, either by mouth or intravenously.

At the time of operation, in all cases except 1 in which there was no obstruction, the bowel was found to be well cleaned out and free from distention. The exception was a case of unobstructed carcinoma of the rectum in which abdominoperineal resection was carried out after the patient had received phthalylsulfathiazole for only three days. In only 1 case, mentioned above, was the drug continued postoperatively, but it is thought that in many cases such continuation could and should be carried out. In support of this may be cited the case of a seventy-eight-year-old man in which a combined abdominoperineal resection was done in one stage after routine preparation. Four days postoperatively the end colostomy slipped back into the peritoneal cavity. The bowel was then retrieved and sutured to the abdominal wall. There was undoubted soiling of the peritoneal cavity, but the patient did not develop peritonitis. He was eventually discharged in a satisfactory condition.

Laboratory Data

Determinations of the blood and urine levels of phthalylsulfathiazole were made daily, as well as red-cell counts, white-cell counts and hemoglobin determinations, in the 19 cases listed in Table 3. No facilities were available for bacteriologic examination of the stools. Such studies have, however, been reported by Poth and Ross,[5] and the effectiveness of phthalylsulfathiazole in reducing coliform and other organisms has been well established.

In Table 3, it will be noted that the daily dose as well as the number of doses varied; this was due to the fact that in these cases an attempt was made to adjust the dosage as accurately as possible to the patient's weight. In view, however, of the extremely low blood concentrations of the drug (measured as sulfathiazole) and in the absence of any toxic manifestations, the simpler routine was thereafter adopted of giving all patients 1 gm. every four hours after the initial dose. In Cases 8 and 14, it will be noted that the blood level was appreciably higher than that in any other case, reaching levels of free drug of 2.040 and 2.681 mg. per 100 cc., respectively. This is due to the fact that these patients were inadvertently given routine doses of sulfadiazine by mouth eighteen to twenty-four hours before these determinations were made.* The figures are interesting in that they show how little phthalylsulfathiazole is absorbed by the blood stream as compared with sulfadiazine.

TABLE 3. *Blood and Urine Concentrations of Phthalylsulfathiazole as Sulfathiazole.*

Case No.	Daily Dose	No. of Doses Daily	Average Blood Concentration		Average Urine Concentration	
			Free	Conjugated	Free	Conjugated
	gm.		mg./100 cc.	mg./100 cc.	mg./100 cc.	mg./100 cc.
1	4.5	6	0.13	0.54	8.8	31.1
2	3.0	6	6.31	0.17	1.2	1.9
3	2.5	5	0.04	0.28	2.5	4.6
4	2.5	5	0.24	0.40	3.5	10.0
5	3.0	6	0.23	0.59	10.7	17.5
6	3.0	6	0.15	0.31	2.3	6.0
7	3.0	6	0.28	0.41	1.5	4.0
8	3.0	6	2.04	2.22	5.8	12.9
9	3.0	6	0.08	0.60	3.6	7.1
10	2.5	5	0.09	0.20	1.4	2.9
11	3.0	6	0.13	0.51	3.9	11.0
12	4.0	4	0.08	0.18	5.2	13.9
13	3.0	6	0.68	0.81	11.9	32.6
14	3.0	6	2.68	14.14	19.6	36.8
15	2.5	5	0.14	0.26	2.9	8.6
16	3.5	6	0.19	0.20	14.1	26.9
17	3.0	6	0.24	0.41	3.6	12.8
18	2.5	5	0.52	0.78	8.4	21.6
19	3.0	6	0.18	0.58	12.3	36.6

Results

There were no toxic reactions from phthalylsulfathiazole in this series.

Among the 49 operative cases — fifty-two operations — in which phthalylsulfathiazole was used

*The routine preoperative use of sulfadiazine as outlined in the section on preoperative preparation was not begun until after the data of the first 19 cases (Table 3) had been collected.

There were 4 cases (8 per cent) with infection. Three patients had wound infection and 1 developed generalized peritonitis and died, a mortality rate of 2 per cent. One of the patients with wound infection received an abdominoperineal resection. The end colostomy slipped back below the peritoneal floor on the fifth postoperative day, but it was almost immediately retrieved, and no peritonitis ensued. A similar accident occurred in another case in which wound infection developed; the mishap was not detected for eight to twelve hours. Colostomy was revised and the patient recovered. These 2 patients had received the drug for four and ten days, respectively, before operation.

The single operative fatality in this group occurred in a patient who had a two-stage operation for carcinoma of the splenic flexure. Following cecostomy, the patient received sulfathalidine for eight days before the second stage of the operation. Extension of the tumor necessitated partial resection of the stomach and splenectomy, as well as resection of the splenic flexure with primary anastomosis. The patient died three weeks postoperatively of peritonitis. The effectiveness of the drug in this case was probably somewhat diminished by the presence of the cecostomy.

Summary

Phthalylsulfathiazole, a new intestinal antiseptic and bacteriostatic agent, after its use in 51 cases was ranked as of definite value as an aid in surgery of the large bowel. Its small dosage, great bacteriostatic activity and low toxicity make it an easy, effective and safe drug to use. Continued use of the drug postoperatively, wherever possible, is advised.

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CHRONIC DISABILITY IN MILD CASES OF TRENCH FOOT

Major Franklin K. Paddock, M.C., A.U.S.

RELATIVELY little study has been made of the persistent signs and symptoms of trench foot and immersion foot, most papers on this disorder dealing with their acute manifestations.[1, 2] According to my experience, however, these symptoms may be disabling for at least one year and are apparently not alleviated by any of a variety of therapeutic measures, including psychiatric treatment. At the present time, with relatively large numbers of patients with this condition awaiting disposition at military hospitals in this country, such a study appears timely.

During February and March, 1945, in Italy, an opportunity was presented to study with special attention some of the manifestations of the later stages of trench foot. These cases, all of which were contracted in the Apennine Mountains of Italy during the winter of 1944–1945, were of mild to moderate severity and were on the whole less severe than those encountered during the preceding Italian winter campaign.

Since the later manifestations of trench foot are typified by subjective complaints most difficult to evaluate, an attempt was made to determine what abnormal responses, if any, could be elicited by various stimuli. In the cases studied, within one or two months after onset, the acute manifestations of edema and gangrene or pseudogangrene had disappeared and spontaneous pain, with tenderness of the soles of the feet, was the chief complaint. The persisting disturbances fell into two main groups — the vascular type, characterized by a tendency to coldness and cyanosis of the feet, and the neural type, marked by pain on firm pressure over the soles of the feet, superficial hypalgesia, loss of proprioception, diminution of temperature discrimination, hyperhidrosis and poor toe-flexion ability.

Vascular Disturbances

It is a frequent observation that patients suffering from the later stages of trench foot tend to have cold, sweaty feet that on dependency rapidly develop cyanosis. The following conclusions were reached from studies of this tendency.

When the shoes and socks of patients with trench foot are removed, the feet are found to be devoid of cyanosis, whether the patients have been stationary or moving about and even though the toe-skin temperatures are usually low (20° to 23°C.). On dependency without the constricting shoes and socks, however, cyanosis generally develops within five minutes. It can be made to disappear by elevating the feet, a normal pink color taking its place. Furthermore, on elevation the cyanotic hue can be readily milked out of the toes. If a uniform light-pressure bandage is applied to a toe when it is pink and the foot is placed in a dependent position, the bound toe is seen to be pink immedi-

ately following the removal of the bandage, even though the remaining toes have become cyanotic. When the foot vessels, either by direct or by reflex methods, have been brought toward full dilatation, as shown by a skin temperature of 30°C. or higher, cyanosis does not appear on dependency so long as vasodilatation, as shown by the skin temperature, persists. With the return of vasoconstriction and cooling of the skin cyanosis develops. If the cyanotic toes are examined through a capillary microscope, it is found that gentle pressure with a glass slide eliminates the cyanosis without obliterating the visible capillaries.

An attempt was made to elicit the so-called "triple response" of the superficial vessels in the distal extensor surfaces of the feet both of normal persons and of those suffering from trench foot. In both groups, the local red response with surrounding pallor was usually obtained by firm stroking with a rounded point, but no wheal or flare was observed in either group. In addition, approximately 0.1 cc. of a 1:1000 solution of histamine phosphate was injected intradermally over the mesial aspect of the first metatarsophalangeal joint of 2 normal persons and of 4 patients with trench foot. In each case a wheal with a surrounding flare of intense erythema appeared after approximately the same interval. This effect could not be reproduced in normal feet by a similar injection of normal saline solution. In the cases of trench foot, with the feet dependent and hence cyanotic, the zone of erythema stood out strikingly against the surrounding cyanotic skin. Simultaneous release of local pressure in both the cyanotic and the erythematous areas revealed a much more rapid return of color to the latter than to the former.

During the winter of 1943–1944, unilateral lumbar sympathetic block in 17 cases of trench foot brought about a prompt rise — within a half-hour — of the skin temperature of the foot on the affected side. This observation was verified in 2 cases during this study, the toe-skin temperature on the blocked side rising to above 30°C. within a half-hour, with cessation of sweating. In 1 case so treated, the intradermal injection of 0.1 cc. of 1:1000 histamine phosphate solution at the bases of both big toes at the height of the vasodilatation brought out prompt wheals with surrounding flares bilaterally.

Effects of Local Heat

The effects of local heat on cases of trench foot were studied by the following method. The left foot was placed in a specially constructed hot-water bath that allowed the foot to be submerged to the level of the malleoli but permitted the tip of the big toe to protrude through a rubber-lined opening so that skin temperatures could be taken. Since it was found by experiment that a minimum temperature of 39°C. was necessary to bring about full vasodilatation, the bath was kept at a temperature of 39 to 40°C. by the addition of hot water. The left foot was kept in the bath until a toe-skin temperature of 30°C. was obtained. When this had occurred, the foot was taken from the bath, dried and placed on a dry bath towel, and skin temperatures were taken at regular intervals for the next half-hour.

Various checks of this method were made. First, the temperature of the surrounding air was taken at regular intervals and found not to vary more than by 2 or 3°C. during any single experimental period, usually being between 21 and 25°C. Secondly, the skin temperature of the right big toe was taken regularly at the same time as that of the left and was found to vary at most by 2 or 3°C. Thirdly, the skin temperature of the thumbs was taken periodically and was found to start at different levels and to vary markedly from patient to patient. No correlation, however, could be found between the temperature of the thumb and that of the left big toe. Fourthly, it was thought that the constriction of the left big toe by the rubber-lined opening might play a significant part in determining its temperature lability. Therefore in the cases that showed markedly delayed vasodilatation by this method, the foot was set in the hot-water bath with the water covering only the lower part of the foot, the tip of the big toe being above water level and free of constriction. The difference between the vasodilatation time obtained by this method and that obtained by the basic method was not significant. Furthermore, the factor of constriction was common to the normal controls and to the patients with trench foot thus tested. Fifthly, the skin-temperature measuring device showed relatively slight variations when tested against a mercury thermometer. Skin temperatures, however, did show variations of as much as 0.5°C., depending on the exact spot on the toe tip tested. An attempt was therefore made to place the filament in as nearly the same spot as possible on each occasion. Lastly, the possible effects of emotional tension on the subjects' neurovascular tone were controlled as well as possible by personal acquaintance with the subject and by reassurance.

The feet of 11 normal persons and of 12 patients with trench foot were studied by this method. In the normal persons, a maximum period of forty-six minutes was required for the skin temperature of the left big toe to reach 30°C. In the cases of trench foot, however, there was a definite trend toward a prolonged vasodilatation time, more than fifty minutes being required to achieve a skin temperature of 30°C. or over in half the cases. In 3 of these cases, furthermore, the toes did not reach this degree of temperature even after having been in the water for eighty minutes. These cases with prolonged vasodilatation time showed a good cor-

*Dermalor, manufactured by the McKesson Appliance Company, Toledo, Ohio.

relation with the tests of reflex vasodilatation (see below) in 3 out of 5 cases.

When the feet were removed from the hot-water bath, no obvious differences occurred in the curves of skin temperature, which was tested over a half-hour period, between the patients and the controls.

Reflex Effects of Heat

The reflex effects of heat were studied by the following method. The patient was surrounded by seven towel-wrapped chemical heating pads* — which may reach a temperature of 90°C. — and was covered by six blankets. Both feet and the left hand were left uncovered. Every five minutes a recording was made of the room temperature, the oral temperature and the skin temperature of the left thumb and of both big toes. The test was considered satisfactory if the oral temperature rose by at least 1°F. or a diffuse diaphoresis occurred within a half-hour period, or if both conditions obtained. If neither of these criteria was satisfied, the test was repeated on another day.

In the normal person, a skin temperature of above 30°C. is said to occur in both thumbs and toes within a half-hour period. In 6 persons so tested, however, the skin temperatures of the big toes reached 30°C. or higher in a maximum of forty-five minutes after the application of heat. For this reason, fifty minutes was taken as the upper limit of normal.

By this method 19 cases of trench foot were studied. In 6 of these, there was failure to reach the required skin temperature within a fifty-minute period, and in 2 of them as much as ninety-five minutes elapsed after the application of heat before this state was achieved.

* * *

The results of these various observations were interpreted as demonstrating certain abnormalities in the neurovascular mechanism of trench foot. It appears that the cyanosis of the feet that develops in dependency is apparently owing to stasis of blood in the venous side of the capillary loops, presumably in the subpapillary venous plexus, and that the cyanosis can be eliminated by an increase in the venous return, effected either by increasing the blood flow through arteriolar dilatation or by increasing the venous tone through extrinsic pressure. Some evidence was also obtained that the capillaries in these relatively mild cases of trench foot are intact.

The results of both the local and the central application of heat were interpreted as showing that at least the more superficial arterioles of the distal portions of the feet have increased tone. Since the paralysis of the sympathetic ganglions regulating those vessels leads to a prompt arteriolar dilatation, it may be assumed that the apparent vascular disturbance lies in reality in the sympathetic nervous system, possibly in the autonomic nerve endings themselves, or that the mechanism is a simple reflex vasospasm such as has been demonstrated in response to painful stimuli. The hyperhidrosis may be taken as further evidence of excessive sympathetic activity.[3] Furthermore, although pathological examinations of the amputated portions of the severer cases of trench and immersion foot have revealed vascular occlusions,[4, 5] there was no evidence in the milder type of case included in this study that any significant intravascular obstruction was present, the arterioles being able to react completely, even if slowly, to appropriate stimuli.

* Kemi-therm, manufactured by the National Mineral Company, Chicago.

Neural Disturbances

Patients suffering from trench foot have difficulty in walking. In almost all cases this difficulty is primarily due to deep tenderness in the feet, which is most marked over the first metatarsophalangeal joint. The patient in placing his foot on the floor usually first throws his weight on the heel and then inverts his foot, so that the weight of the body as it moves forward is distributed along the lateral margin, the ball of the foot touching the ground last and only gently. The toes are generally held in a cocked-up position. The gait tends to be shuffling.

Neurologic examination of these feet in almost all cases reveals superficial hypalgesia to pinprick involving at least the flexor surface of the big toes. The more extensive areas of hypalgesia may have a narrow zone of hyperalgesia at their proximal border, and in an occasional case the superficial sensation of the whole distal portion of the foot is hyperalgesic. Hypesthesia or anesthesia to light touch is found too frequently in the toe tips of military personnel to admit comparison with cases of trench foot. Proprioception of the toes, as evidenced by position and vibration sense, may be diminished or absent. In 33 patients studied particularly for this phenomenon, 13 had poor position sense and 8 had absent vibratory sense of the big toes.

An occasional patient shows diminished or absent ability to flex the toes voluntarily. This has been noted in the earliest stages of trench foot while the patient was still bedridden. Of 33 patients with trench foot examined with this especially in mind, 8 had poor toe-flexion ability. A more careful analysis of this disability indicates that the fault lies not in the short but rather the long flexor muscles, since flexion is absent in the distal rather than in the mesial or proximal phalanges. In all cases the toes could be flexed by the examiner with ease, and in most cases this caused no obvious discomfort. This disability showed no definite correlation with loss of proprioception sense but did show some correlation with the severity of the disease, being more frequent in the severer cases.

Galvanic and faradic stimulation* of the long extensor and the long and short flexor muscles of the toes and faradic stimulation of the plantar nerve were carried out on 7 patients with trench foot, who showed diminished to absent ability to flex the toes. The same average quantity of ohms in the galvanic stimulation and of volts in the faradic stimulation brought the same threshold response in the patients with trench foot as it did in a similar number of normal persons. With these results in mind, 2 intelligent and co-operative patients with trench foot who had poor toe-flexion ability — one unilaterally — were given daily re-education in toe motion. At the end of five days both patients were able to flex the terminal phalanges of the big toes voluntarily. They had been in the hospital for sixty to ninety days at the time this experiment was tried without regaining this ability by themselves.

The ability to distinguish between hot and cold was tested. With the use of test tubes filled with warm and with cool water, with a temperature difference between them of 15 to 20° C., 21 normal persons and 14 patients with trench foot were examined, the test tubes being held for a maximum of five seconds against the area in and around the big toes. In all cases of trench foot so tested there was a loss of temperature sense in at least the tips of the big toes, whereas in the normal persons — except in 1 case complicated by marked toe callus — there was a ready ability to distinguish the temperature difference. In addition, a minority of the patients with trench foot had this loss at the base of the big toes on both the flexor and extensor surfaces. In all the cases of trench foot except 1, hypalgesia began proximal to the area of loss of temperature sensation. There seemed to be no correlation between proprioception and the extent of temperature loss, in that position sense might be present even when there was a loss of temperature sensation over the entire big toe.

An attempt was made to demonstrate the presence or absence of deep-seated sensitivity to cold in the distal portions of the foot in cases of trench foot. The subject was seated in a chair with the toes and ball of one foot and the fingers of one hand submerged in a pan of ice water. Since higher temperatures gave equivocal results in normal persons, the temperature of the water was kept at about 5°C. The members were kept submerged for a minimum of ninety seconds.

Ten patients with mild to moderate cases of trench foot and 10 normal persons were tested by this method. All the patients with trench foot complained of aching of the fingers within one minute, but only 1 complained of aching in the submerged portion of the foot. All the normal persons complained of aching of the foot, but in most cases the pain was confined to the areas of the metatarsophalangeal joints and was not of sufficient severi to make the subject withdraw his foot from the bat

* * *

Either loss or exaggeration of superficial pa over the more distal portions of the feet appears be common to all cases of trench foot. Loss proprioception may occur in some cases, but de pain sensation tends to persist. Loss or diminut of temperature sensation is a frequent findi Since it is said that in a cooled nerve the sense warmth is lost before that of coldness,[6] it was hop that these observations would help to distingui between nerve damage caused by cooling and th caused by asphyxia. No conclusions in this rega however, could be drawn.

It has been stated that the deep-seated achi due to cooling of an extremity is mediated by t small nonmyelinated nerve fibers of Class C.[7] T absence of this pain in cases of trench foot is eviden that these fibers are damaged. Although the abo study tends to show that such damage has occurr the method is in essence dependent on subjecti interpretations of pain and hence is not particula valuable as a test for this condition.

The loss of voluntary toe flexion found in so cases is rather difficult to understand. The mo nerves and muscles show no obvious functional structural abnormality. It seems likely that t disability is due to a disturbed toe-flexion patte perhaps lost during the earliest stages of the dise when acute edema and vascular disturbance m toe motion painful.

Pathology

Scattered reports of the pathology of this con tion are available in the literature.[4, 5] In sev cases, gangrene with complete or partial vascu obstruction is obvious. Intense fibrosis and creased deposition of collagen have been descri in severe cases of immersion foot.[8]

In 3 of the mild cases examined in this stu biopsy specimens of the tissues overlying the me aspect of the proximal phalanx of the big toe w taken. Microscopical examination† of secti stained with the Bodian protargol method reve minor changes in the nerve trunks consisting focal swelling of the axone cylinders. The ner appeared to contain a comparatively large amo of fibrillar tissue for the location and the numbe Schwann-cell nuclei. The vessels, corium epidermis appeared normal, and there was no dence of an increase in fibrosis or collagen or decrease in fat.

Comment

The chronic disability resulting from mild tre foot presents an interesting problem. In the e stages of the disease, damage to the blood ves

*This was done with the technical assistance of First Lieutenant Helen T. Lawrence, physiotherapist.

†These examinations were interpreted by Major Victor N. Tom M.C., A.U.S.

resulting in inflammatory edema and a tendency to gangrene, overshadows the other aspects of the condition. When this phase has subsided, the patient is left with painful, tender feet that have a tendency to become cyanosed on dependency or exposure to cold. On gross examination in a warm room with the legs horizontal, the feet appear completely normal, and only on neurologic examination of the distal portions of the feet does any abnormality become apparent. When cyanosis is induced, vascular disease is at once assumed and is considered to be responsible for the disability. From the observations in this study, however, this does not appear to be the case; rather it is the terminal nerve twigs that are at fault — a terminal neuritis. Furthermore, one occasionally encounters a supposedly normal person whose extremities become cyanotic under similar conditions but who does not complain of any pain or tenderness such as that experienced by patients with trench foot. It is because neuritis is the underlying fault that, at least in my experience, interruption of the sympathetic pathways to the feet does not bring about frank relief of the symptoms, although it relieves the cyanotic tendency — and, of course, the associated hyperhidrosis.

On the basis of prolonged observation of these patients in the Mediterranean Theater of Operations, it has been found that the complaints of pain and tenderness clear extremely slowly. During the summer, hyperhidrosis, with resultant skin maceration and a tendency to epidermophytosis, was frequent. The pain and tenderness felt on walking was less during the warm weather, but even so prevented the sufferer from taking long marches. During the subsequent winter, a year after the onset of the disease, when the weather was cold and damp, spontaneous aching occurred and was associated with further diminution of walking ability, although not to its initial levels. It appears likely that this disability will disappear only after a period of years and that therapy directed at the blood vessels and non-neural tissues will be of no avail.

Summary and Conclusions

A study was made of the later manifestations of trench foot of relatively mild severity.

A variety of related observations of the arterioles, capillaries and venules revealed that there was increased arteriolar tone, apparently secondary to increased sympathetic stimulation, but no evidence of arteriolar obstruction. The capillaries and venules were apparently normal.

Observations of the sensory and motor nerve disturbances revealed that besides superficial hypalgesia there was frequently diminution of temperature, vibration and position sense. Poor toe-flexion ability was shown to be owing to no obvious structural abnormality. Deep-seated sensitivity to cold tended to be absent.

The lesions of the less severe cases of trench foot are conceived of as involving all the more superficial foot tissues, but with a quantitative variation from patient to patient as regards the tissues affected. It appears that the disability encountered in the later stages of mild cases of this condition are more dependent on neural than on vascular disease. Microscopic examination of the damaged tissues tends to confirm this concept.

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HEMORRHAGE FROM THE GALL BLADDER*

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THE purpose of this paper is twofold — to present 4 cases of hemorrhage into or from the gall bladder, 3 of which had unusual features, and to show the significance of hemorrhage into the gastrointestinal tract in cases of cholelithiasis, as indicated by routine examination of the stools.

Of the cases of massive hemorrhage from the gall bladder, 1 was due to neoplasm, so that the hemorrhage was not remarkable. The other 3 cases, however, are similar to the 24 already contained in the literature. This condition was first reported in 1892 by Naunyn,[1] who described 3 cases of ruptured arterial aneurysms causing massive hemorrhage into the gall bladder. In 1903, Huguein[2] reported a case of such a hemorrhage into the gall bladder and throughout the extrahepatic billiary duct system, but this was found to have been caused by carcinoma of the common duct. In 1915, Schnyder[3] reviewed the literature and found 8 cases similar to those presented here, and added 2 of his own. In 1925, Heusser[4] reported the case of a forty-seven-year-old man with cholelithiasis who developed massive hemorrhage into the lumen of the gall bladder. Perhaps the most remarkable case contained in the literature is that given by Fiessinger et al.[5] His patient was a four-year-old child who developed massive idiopathic bleeding from a noninfected gall bladder that contained no stones. In 1939, Meyer–May[6] reported a case of enormous hemorrhage into the gall bladder that was probably due to trauma incurred in a football game.

Another group of hematocholecysts found in the literature are those reported by Leared[7] in 1858, Schnyder[3] in 1915, Gjellerup[8] in 1921, Waters[9] in 1926, Bartlett and Bartlett[10] in 1936 and Mailer[11] in 1939. In all these cases there was spontaneous rupture of the gall bladder, with considerable free intraperitoneal hemorrhage. Each case represented a mechanical tearing of the wall of the gall bladder secondary to blockage of the cystic duct. These cases, together with those of traumatic hemorrhagic cholecystitis, such as that described by Ireneus,[12] are not considered to be similar to the cases reviewed and reported elsewhere in this paper.

Hemorrhage into the gastrointestinal tract, as indicated by routine stool examination, is of importance in cases of cholelithiasis. In a number of patients in whom anemia is apparently the primary disease, little attention is directed to the biliary system. It has long been well known, if not fully appreciated, that a considerable percentage of patients with cholelithiasis have no marked abdominal symptoms or signs. A considerable number of them have blood in the stools, a point that is frequently neglected in the differential diagnosis. In reviewing our own cases, it was found that in 13 per cent of 100 consecutive cases of cholelithiasis brought to operation there was blood in varying amounts in the stools. In some of the cases there was concomitant disease, which may or may not have been the cause of melena. For instance, a patient had had a duodenal ulcer excised twenty-four years previous to admission for cholelithiasis. At the earlier admission, however, there was no blood in the stools. Another patient had diverticulosis of the colon, which may or may not have accounted for the presence of blood. Other disease, such as carcinoma of the breast, may be discounted as noncontributory to the finding of blood in the stools. In cholecystitis without cholelithiasis, 8 per cent of the cases with this finding in a series of 100 consecutive cases have been operated on at the Beverly Hospital in recent years.

CASE REPORTS

CASE 1. S. S. (No. 54359), a 57-year-old, Jewish housewife, had had several previous hospital entries. Twenty-two years prior to admission she had a resection of the left ovary, left salpingectomy, right salpingo-oophorectomy, ventral fixation of the uterus, perineorrhaphy and dilatation and curettage. Fifteen years after the initial operation, she had a second perineorrhaphy and also an anterior colporrhaphy. Up to eight months prior to this admission the patient was in good general physical condition except for a 7-year history of occasional attacks of asthma. A careful history-taking, however, revealed that as long as 1 year prior to admission she had had a sense of fullness in the epigastrium after eating. This usually occurred directly after taking a meal and was never accompanied by actual abdominal pain, although there was considerable gaseous distention. Some relief was obtained from the ingestion of sodium bicarbonate. There was no history of nausea, vomiting, jaundice, dark urine or tarry, bloody or clay-colored stools.

Eight months before the patient entered the hospital, she developed pain radiating from the substernal region to the back, especially on the left side, and extending into the arms. At that time a diagnosis of coronary disease was made and treatment was given accordingly. Shortly thereafter, because of an idiopathic anemia, the patient was given iron and liver therapy and placed on a special diet. One month later she began to have tarry or black stools. This may have been due to the oral administration of iron, because during 1 week of abstinence from iron the stools became brown. Four months later, during a stay at this hospital for bronchial asthma, hypertrophic arthritis, secondary anemia, possible gall-bladder disease and coronary insufficiency with healed myocardial infarct, the stools revealed a +++ test for occult blood, the reason for which was not immediately explained. A moderate secondary anemia with a hematocrit of 30 per cent quickly resulted. Extensive x-ray study of the gastrointestinal tract and gall bladder revealed no gastrointestinal cause for the melena, but the gall bladder was seen to be diseased. An attempt by an internist to determine the cause of secondary anemia following discharge also failed. Tenderness in the right upper quadrant of the abdomen,

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unexplained melena and secondary anemia continued, the anemia progressing until the red-cell count was 2,000,000 and the hemoglobin 40 per cent. There were four admissions for transfusion only during the 2 months prior to the final admission. This procedure was necessary because the patient persistently refused an exploratory laparotomy that the surgical staff advised on the basis of x-ray evidence of gall-bladder disease, together with bleeding from the gastrointestinal tract.

Physical examination on admission revealed a well developed, somewhat obese, moderately ill, woman complaining of pain in the right upper quadrant of the abdomen. She was not cyanosed, dyspneic or jaundiced. The temperature was 101°F., the pulse 92, the respirations 22, and the blood pressure 140/80. The abdomen was slightly obese but not distended and contained a well healed scar low in the midline. The liver edge was palpable 3 fingerbreadths below the costal border at the right midclavicular line. Just below the liver edge there was felt a dome-shaped mass 2 cm. in diameter that was exquisitely tender. The mass was freely movable but seemed to move synchronously with the liver on deep breathing. The kidneys were not palpable, nor was the spleen. No other masses were felt. No hernia was demonstrable. There was no appreciable rebound tenderness or muscle spasm.

The urine was essentially normal except for the presence of sugar. The hemoglobin was 55 per cent, the red-cell count 2,610,000, and the white-cell count 6350, with 77 per cent neutrophils, 21 per cent lymphocytes and 2 per cent monocytes. The reticulocyte count was 1.1. A blood smear was not remarkable. The total protein was 7.4 gm. per 100 cc. The albumin-globulin ratio was 1.4. The blood nonprotein nitrogen was 34 mg. per 100 cc., and the blood-sugar level 140 mg. The patient at that time was taking 40 units of regular insulin daily. The blood Hinton reaction was doubtful. The hematocrit was 32 per cent.

X-ray examination of the gastrointestinal tract was negative. Examination of the gall bladder after the administration of dye led to a diagnosis of pathologic gall bladder.

During the hospital stay the patient was transfused several times, beginning immediately after admission. On the 3rd hospital day, with a preoperative diagnosis of an abdominal mass in the right upper quadrant, of undetermined source and nature but probably malignant, mild, uncomplicated diabetes mellitus and unexplained melena, a laparotomy was performed through an incision in the right upper rectus muscle. The gall bladder was distended and filled with stones and large blood clots. The liver was enlarged but was otherwise not remarkable. Cholecystectomy and biopsy of the liver were carried out. The common duct was not explored. The patient was transfused after operation. Postoperatively the temperature spiked to 101.5° F. on several days, but otherwise improvement was steady. The drain was removed on the 8th postoperative day, following which the temperature rose and a small wound abscess developed, a culture of which grew *Staphylococcus aureus*. Following this mild complication, recovery was uneventful. The diabetes was controlled fairly well with insulin and diet. The stools showed no further blood. The pathological report revealed chronic cholecystitis with cholelithiasis and a malignant hemangioendothelial sarcoma. Apparently this lesion had been removed in toto. There was no evidence of metastasis at operation, and there has been no recurrence of symptoms, or anemia.

Comment. This case at first seems to support the belief that bleeding from the gall bladder is prone to occur in patients with vascular disease. The patient was diabetic, and although she had no marked external arteriosclerosis, there was a history of coronary insufficiency and she was at an age when diabetic arteriosclerosis begins to manifest itself. The presence of the hemangioendothelial sarcoma within the gall bladder, however, may well have accounted for the bleeding. This finding actually seems to exclude this case from the group of true hematocholecysts to which the other 3 cases presented here clearly belong.

Case 2. D. W. (No. 26893), a 30-year-old housewife, was admitted 9 years after an initial attack of severe epigastric pain. Other attacks subsequently occurred, and in all of them the pain was constant and acute in onset. A similar attack 6 months prior to admission had lasted for only 1 hour. The present attack centered in the right upper quadrant of the abdomen, and the patient ascribed her symptoms to ice cream that she had eaten a few hours previously. She had vomited bile-colored fluid many times. She had never been jaundiced and had noticed no tarry or clay-colored stools or dark urine. She had passed no gross blood with stools.

Physical examination revealed an obese woman with acute distress in the upper abdomen. The temperature was 98.2°F., the pulse 76, and the respirations 20, and the blood pressure 120/80. The abdomen was obese but soft. There was marked tenderness in the right upper quadrant and throughout the entire epigastrium. There was no rebound tenderness, no palpable mass, and no hernia or other pathologic findings. Peristalsis was normal.

The urine was essentially normal. The hemoglobin was 97 per cent, the red-cell count 4,940,000, and the white-cell count 16,900 with 79 per cent neutrophils, 18 per cent lymphocytes, 2 per cent monocytes and 1 per cent eosinophils. The stool was brown and contained no blood. The icterus index was 8.2. The van den Bergh reaction was indirect. The bilirubin was less than 2 mg. per 100 cc. A blood Hinton test was negative. In a test for urinary diastase, 32 cc. of starch solution was digested by 1 cc. of urine. The blood nonprotein nitrogen was 26 mg. per 100 cc., and the blood sugar 80 mg.

Three days after admission, x-ray examination of the gall bladder following intravenous administration of dye revealed no concentration of dye. No stones were visible. An x-ray diagnosis of pathologic gall bladder was made.

On the 5th hospital day, with a preoperative diagnosis of acute cholecystitis and cholelithiasis, a laparotomy was performed under spinal anesthesia through an incision in the right upper rectus muscle. The gall bladder was moderately distended, and the mesentery was adherent to it. On aspiration of the gall bladder a large amount of fresh gross blood was obtained. There were several faceted stones and two ulcerations in the mucosa. No exploration of the common duct was carried out. The pathological diagnosis was the subsiding phase of a chronic recurrent cholecystitis and cholelithiasis, with formation of small ulcers. The postoperative course was uneventful, and the patient was discharged on the 15th postoperative day.

Comment. This case is probably typical of the cases of cholecystitis with cholelithiasis in which there is unexplained hemorrhage into the gall bladder. There was no blood dyscrasia and no known vascular disease, but microscopic sections of the extirpated gall bladder revealed marked sclerotic changes in the blood vessels.

Case 3. H. R. (No. E-4154), a 68-year-old housewife, was admitted with a chief complaint of acute epigastric pain radiating to the back. Pain had begun on the previous day. The patient had had "gall-bladder trouble" during the 24 years prior to admission. The attacks, which lasted for 10 to 15 minutes and occurred several times yearly, consisted of discomfort in the midepigastrium, with radiation of dull pain to the right costal margin and beneath the right shoulder blade. There was also a sensation of gaseous distention. Between attacks there was a slight degree of indigestion, characterized by gaseous distention following meals. The patient generally refrained from fatty foods but found that she could occasionally take fat in small amounts. There was no history of jaundice, dark urine or clay-colored or tarry stools prior to the most recent attack. There had never been chills.

Twelve years prior to admission the patient was seen at a diagnostic clinic, where she was told that she had "gall-bladder trouble." She was not operated on, since it was thought desirable to reduce the body weight, which was well over 200 pounds, before surgery was attempted. Six weeks before admission, she had an unusually severe attack, accompanied for the first time by mild nausea and vomiting. X-ray films taken elsewhere revealed impaired function of the gall bladder. There was no jaundice with the present attack, but the urine was mahogany-colored. The bowel movements had been scanty and clay-colored for the last few days. There was no history of diarrhea, blood in the stools or tarry stools.

Physical examination on admission revealed an obese

woman in moderate epigastric distress. There was a slight icteric tinge to the skin and scleras. The temperature was 98°F., the pulse 100, the respirations 20, and the blood pressure 186/104. The abdomen was soft and nontender. No masses were palpable in any quadrant, nor was there muscle spasm.

In a test for urinary diastase 4 cc. of starch solution was digested by 1 cc. of urine. The blood nonprotein nitrogen was 28 mg. per 100 cc. and the blood sugar 87 mg. The icterus index was 17. The van den Bergh reaction was immediate and indirect. The bilirubin was 2.89 mg. A blood Hinton test was negative. The prothrombin time was 35 seconds (normal, 17 seconds). The blood amylase was 45 mg. per 100 cc. The stool revealed a ++++ test for blood, and the vomitus a +++ test. The urine gave a ++ test for bile, the sediment contained a few red and white cells and bacteria. The hemoglobin was 71 per cent, the red-cell count 3,740,000, and the white-cell count 8400, with 68 per cent neutrophils, 30 per cent lymphocytes and 2 per cent monocytes. A blood smear was not remarkable.

The electrocardiogram was negative except for mild left-axis deviation, which was ascribed to left ventricular hypertrophy.

During the hospital stay there were recurrent attacks of nausea, vomiting and upper abdominal pain. Most of the stools contained blood. The bile disappeared from the urine 9 days after admission.

A preoperative diagnosis of chronic cholecystitis, cholelithiasis, choledocholithiasis and hemorrhage from the gall bladder was made. Under spinal anesthesia, a laparotomy was performed through an incision in the right upper rectus muscle, and an adherent gall bladder containing large clots of gross blood and numerous stones was removed. There were two ulcerations in its mucosa. The common duct contained three stones. The pancreas was normal. No other disease was found in the right upper quadrant of the abdomen. A T-tube was placed in the common duct, and a large amount of bile drained postoperatively. The postoperative course was uneventful, and the patient was discharged on the 23rd postoperative day. The pathological diagnosis was chronic and acute cholecystitis, cholelithiasis and blood clot in the gall bladder. There was no evidence of malignancy.

Comment. This case was remarkable in that extensive studies were undertaken to determine the exact cause of bloody stools that coexisted with known cholelithiasis and cholecystitis. By a process of exclusion, the only feasible explanation for the presence of blood in the stools was bleeding from the gall bladder, so that this diagnosis was made preoperatively. Such a diagnosis is highly unusual in the medical literature on this subject.

This patient suffered from hypertensive and arteriosclerotic heart disease of a mild sort, and it is known that bleeding from the gall bladder is likely to occur in patients with arterial and venous disease. Heusser[4] points out that the real reason for hemorrhage from the gall bladder is probably intrinsic pathologic changes in blood vessels rather than direct or mechanical erosion of the vessels by stones. Microscopic studies of this case seemed to confirm this theory.

Case 4. W. C. (No. J-4033), a 44-year-old man was admitted with a history of attacks of sharp pain in the right side of the chest, accompanied by nausea and four spells of vomiting, of 5 days' duration. The vomitus consisted of undigested particles of food. Following the pain in the chest there was dull pain in the right upper quadrant of the abdomen, which persisted and became worse shortly before admission. During the 48 hours prior to admission, the nausea and vomiting subsided. The patient had been treated for 3 days by his local physician, the treatment consisting of bed rest and nothing by mouth except whisky and water. The patient had never been jaundiced and had never noticed clay-colored, tarry or bloody stools. His past history revealed nothing remarkable except constipation during the week prior to admission. There had been no previous surgical operations or hospitalizations.

Physical examination on admission revealed a stocky, well developed and well nourished middle-aged man in mild upper abdominal distress. He was alert and co-operative and was not cyanotic, dyspneic or jaundiced. The temperature was 99°F., the pulse 88, the respirations 20, and the blood pressure 152/82. The heart was enlarged to the left and downward. The apex impulse was felt in the 6th intercostal space outside the midclavicular line. The heart sounds were of good quality, and the rate was regular. There were no thrills or murmurs. The abdomen was obese. There was exquisite tenderness around the region of the gall bladder in the right upper quadrant, where a large mass, assumed to be a distended gall bladder, was readily palpated. The spleen and kidneys were not felt. There was no evidence of hernia. Peristalsis was normal. The rest of the abdomen was soft and nontender. There was no demonstrable fluid. An admission diagnosis of subsiding acute cholecystitis and cholelithiasis was made.

The urinalysis was negative except for the presence of 30 to 40 white cells per high-power field in the sediment. The red-cell count was 5,030,000 and the hemoglobin 97 per cent. The white-cell count was 10,350, with 79 per cent neutrophils, 16 per cent lymphocytes, 2 per cent monocytes and 3 per cent eosinophils. A blood smear was not remarkable. Examination of the stool revealed mucus but no blood. A blood Hinton test was negative. The nonprotein nitrogen was 28 mg. per 100 cc., the blood sugar 77 and the vitamin C level 0.35 mg. The total protein was 5.9 gm. per 100 cc., the fibrinogen being 0.7 gm., globulin 2.1 gm. and the albumin 3.1 gm., an albumin-globulin ratio of 1.5.

X-ray examination confirmed the presence of gallstones, and on the 3rd hospital day, under spinal anesthesia, the abdomen was opened through an incision in the right upper rectus muscle. The gall bladder was found to be greatly distended, and stones were palpated in it. There were no ulcerations in the serosa. Cholecystectomy was carried out without undue difficulty, and the patient had an uneventful postoperative recovery until the 4th postoperative day, when the lower end of the rectus incision opened and there was a slight evisceration of omentum through the wound. Resuturing was immediately carried out under spinal anesthesia. Following this, no further complications developed, and the temperature did not rise above 99.6° F. after the second operation.

When the gall bladder was opened following operation, it was found to contain several clots and a massive hemorrhage. There were also present the pathologic changes suggestive of chronic and acute cholecystitis, as well as gallstones. A pathological diagnosis of bleeding gall bladder revealing a marked chronic and acute inflammatory process was made. The microscopic examination of sections from the gall bladder revealed the mucosa to be swollen and edematous and the blood vessels to be markedly dilated. The sclerotic changes in the vessels described in Cases 2 and 3 were present but not marked.

Summary

The literature on hemorrhage of the gall bladder is briefly reviewed, and 3 cases of idiopathic hemorrhage are reported. A case of hemorrhage from hemangioendothelial sarcoma of the gall bladder is also described.

It seems quite likely, after reviewing our operative cases and those collected from other workers, that sclerotic changes in the vessels of the gall bladder are the underlying cause of such hemorrhage. Mechanical irritation from stones seems to be a secondary consideration.

The only lesson to be learned from these case studies is that more attention should be directed to the finding of blood in the stools of patients in whom cholelithiasis has not been excluded. It is probable that many cases of unexplained secondary anemia or of blood in the stools are due to cholelithiasis.

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CLINICAL NOTE

SENSITIVITY TO TINCTURE OF MERTHIOLATE

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TINCTURE of Merthiolate is widely used as a skin antiseptic and a preoperative preparation. This tincture is a 1:1000 alcohol acetone aqueous solution of sodium ethyl mercurithiosalicylate. Sensitivity to it is rare, but because this may occur and cause a disabling dermatologic complication, the present report seems justified.

CASE REPORT

A 21-year-old soldier was admitted to the 101st General Hospital on April 14, 1945. Three weeks previously, he had fallen from a vehicle suffering abrasions of both knees. After 5 days of self-treatment by dressing the abrasions with his first-aid packet, without noticeable improvement, the patient reported to the dispensary, where the abrasions were painted with Tincture of Merthiolate. This treatment was repeated daily for 5 days, by which time the skin had blistered, so that the treatment was stopped. The skin lesions, however, became more disabling during the next few days, and the patient was sent to this hospital. As a civilian he had had numerous attacks of poison-ivy dermatitis.

At physical examination the patient did not appear to be seriously ill. The extensor surfaces of both knees and the adjacent thigh and leg areas were the sites of a secondary infected dermatitis. There were many blebs and bullae, filled with serous or purulent fluid, and inflammatory erythema and induration were present throughout the area of involvement.

Patch tests were done in the usual manner on the flexor surfaces of the forearm with the following substances: Tincture of Merthiolate; aqueous Merthiolate solution; alcohol; acetone; Tincture of Metaphen (4-nitro-anhydro-hydroxymercury-ortho cresol); aqueous solution of Mercurochrome (dibrom-oxymercuri-fluorescein-sodium); and mercurial ointment (30 per cent metallic mercury). In the test with Tincture of Merthiolate, the patch had to be removed in 12 hours because of severe pruritus. The reaction exactly mimicked the lesions on the knees, showing blebs, vesicles and induration, and it spread to involve an area five times the size of the patch. Two weeks later, evidence of the reaction still remained (Fig. 1). A reaction of equal severity resulted from the test with the aqueous solution of Merthiolate. All the other patch tests were negative after 48 hours.

The lesions were treated as those of a pyoderma and cleared up without difficulty. Considerable discoloration persisted.

The material used for the patch test, which was performed in England, was not the same as that originally applied to the knees. The mercurials other than Merthiolate elicited no reaction and the tests with acetone and alcohol were similarly negative. All the tests were applied to areas not previously treated by any other drug. One must conclude that the sensitivity was due specifically to Merthiolate, since there were positive reactions both to the tincture and to the aqueous solution.

FIGURE 1. *Photograph of the Reaction.*
This photograph was taken two weeks after the patch test with Tincture of Merthiolate had been applied.

SUMMARY

An unusual case of skin sensitivity to Merthiolate is presented. No sensitivity to other mercurials could be demonstrated. Because of the widespread use of this skin antiseptic, the possibility of such sensitivity should be kept in mind.

MEDICAL PROGRESS

DIABETES MELLITUS

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THIS review of progress in diabetes mellitus will consider advances in knowledge concerning alloxan and carbohydrate metabolism, recent papers on diabetic neuropathy, two articles dealing respectively with diabetes in children and with facts concerning the disease in Finland and, finally, associations, societies, foundations and trusts primarily interested in the problems brought about by this disease.

ALLOXAN

Duff,[1] a well informed scientific investigator whose opinion is greatly respected and whose review of the pathology of the pancreas in experimental diabetes mellitus is most complete, makes the following statement: "It is most improbable at present that alloxan plays a role in the etiology of human diabetes." Despite this assertion, I cannot escape the clinical conviction that the discovery of the specific action of this substance in destroying the beta cells of the islands of Langerhans has brought medical scientists nearer to the explanation of diabetes than has any step made hitherto — including partial pancreatectomy and the injection of anterior-pituitary extract. Since the progress reports of 1944 and 1945 in this journal,[2, 3] distinct advances have been made in the knowledge of alloxan that strengthen this belief. More and more the specificity of its action in animals and birds has been confirmed. Although in the human body alloxan has not been demonstrated in metabolic processes, particularly that of uric acid, from which it can be derived, tests for it have identified its presence in the tissues of animals.

The first of these tests was devised by Leech and Bailey.[4] It detects alloxan in quantities as small as 0.05 mg. in blood, and with slight modifications in certain tissues, including the pancreas. It has been found that alloxan reaches its highest level at the end of injection, following which it rapidly decreases, with complete disappearance from the blood in five minutes. It is found in the tissues of the pancreas in quantities of 24 to 56 mg. per 100 gm. at the end of the injection.

A second test, devised by Banerjee, Dittmer and du Vigneaud,[5] involves the conversion of alloxan into riboflavin, a phenomenon that is measured by microbiologic and fluorometric technics. It is useful only for the detection of alloxan in aqueous solutions. These authors confirmed the results of Leech and Bailey regarding the stability of alloxan at various hydrogen-ion concentrations. They showed that alloxantin, which acts similarly to alloxan, yields the same amount of riboflavin as does alloxan. Incidentally, the fact that alloxan and alloxantin are closely akin to a vitamin is interesting, even if not yet proved to be significant. Moreover, if alloxan can be converted into riboflavin, the reverse may well be possible.

Ruben and Tipson,[6] in a preliminary paper, have recently reported the detection by another method of what they assumed to be alloxan in the normal livers of the steer, cat, calf, domestic fowl, guinea pig, lamb, rabbit and rat.

Finally, Archibald[7] has described six methods for the detection of alloxan under varying conditions. As a result of his tests, he concludes that the blood plasma and urine of normal human beings and dogs must contain less than 0.02 mg. of alloxan per 100 cc. The addition of alloxan to filtrates of whole blood containing glutathione results in the formation of dialuric acid. Archibald states that the possibility that circulating blood normally contains small amounts of alloxan should not be overlooked.

These various tests for alloxan and the demonstration of its existence and reactions under varying conditions in animals count toward its conceivable importance in diabetes.

Substances closely akin to alloxan act similarly to it. The first of these is alloxantin, which was referred to in my last progress report.[3] Styryl quinoline No. 90, which was originally found by Dunn to destroy the islet cells, has not as yet been proved to cause diabetes, but Bruchmann and Wertheimer[8] have shown that methylalloxan, dimethylalloxantin, dialuric acid and methyl dialuric acid produce it in rats when injected intravenously. The demonstration that these bodies, so closely related to alloxan, also cause diabetes suggests that if the search is continued, the actual chemical that plays the diabetogenic role can be found.

Neutralized alloxan or alloxan dissolved in either rabbit or human blood plasma is not diabetogenic. This discovery, of which I was aware a year ago, has now been published by Leech and Bailey.[4] Weinglass, Frame and Williams[9] have gone a step farther and shown that 3-4, diamino-toluene, orthophenylene-diamine or sodium bisulfite, if injected intravenously within five minutes before alloxan is given,

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prevents its diabetogenic action. A marked decrease in the blood glutathione invariably follows the injection of a diabetogenic dose of alloxan.[10] When the molecular equivalent (400 mg. per kilogram of body weight) of reduced glutathione is injected immediately before and during the injection of 200 mg. of alloxan per kilogram of body weight, the glutathione fails to prevent the subsequent diabetes. The blood-alloxan and blood-reduced-glutathione determinations made in 6 rabbits injected with 200 mg. per kilogram suggest that there is an immediate reaction between alloxan and blood-reduced glutathione, with a tendency toward the complete disappearance of both. The critical level at which blood-reduced glutathione changes tend to parallel the development of diabetes is about 100 mg. per kilogram. During the slow development of diabetes through repeated small doses of alloxan, the blood-reduced glutathione tends to be increased over normal, with a sudden drop to normal as diabetes ensues.[4]

The rapidity of the action of alloxan in causing destruction of the islets of Langerhans and producing diabetes is so unlike the speed of development of the disease in human beings that the demonstration by Bailey, Bailey and Leech[10] that repeated doses over a long period also bring on the disease naturally appeals to a clinician. This rapid destruction of the islets by a single large dose of alloxan, however, was shown by Goldner[11] and Gomori and Goldner[12] when they temporarily ligated the blood supply to half the pancreas and injected alloxan. The temporary ligatures were released five minutes later, and histologic sections revealed the absence of changes in the islet cells in the part of the pancreas deprived of blood for this period of time, whereas in the remaining portion the usual necrosis of the islets was present.

Marked differences exist between alloxan diabetes and the diabetes caused by partial pancreatectomy and the injection of anterior-pituitary extract. In the former particularly, the disease can be prevented or even cured if hyperglycemia is avoided; this is distinctly not the case with alloxan diabetes. Differences in the pathologic picture have been emphasized by Duff[1] as follows:

> The hydropic degeneration of the beta cells produced by partial pancreatectomy appears to be identical with that produced by anterior-pituitary extracts. This change is at first reversible and only later progresses to irreversible cell damage. In both instances hydropic degeneration is probably caused by the excessive functional demands associated with hyperglycemia. . . . In alloxan diabetes, the beta cells of the islets show, from the beginning, degenerative changes that lead quickly to necrosis without the appearance of a stage in any way resembling hydropic degeneration. The necrosis is probably caused by the direct action of alloxan on the islet cells, and this injury is irreversible.

It should not be overlooked, however, that there are resemblances between alloxan diabetes and the diabetes caused by partial pancreatectomy and anterior-pituitary extract. Thus, Bailey, Bailey and Leech[10] found that in the diabetes produced in one to three weeks by the daily injection of small doses of alloxan (40 mg. per kilogram of body weight), the pancreas underwent a series of changes quite different from those following a single massive injection. With the small doses a wide variety of changes in the beta cells was apparent. Some of them looked almost normal, whereas in others degranulation was the only evidence of injury, and still others showed hydropic degeneration. On the other hand, these authors also state, "This complex picture of normal cells, slightly injured cells, cells with hydropic degeneration, irreversibly damaged cells and a mitosis in a single islet is not clearly duplicated in any other form of experimental diabetes or in human patients," but I have always understood this statement to mean that in these animals a remarkably comprehensive picture in a single islet can be found for which one would need to search in several islets in the human being.

Hughes and Hughes[13] injected rats subcutaneously with repeated small injections of alloxan. They found that the larger and presumably older beta cells of the pancreas succumbed to the toxic action of concentrations of alloxan that were too low to damage young beta cells.

Further studies on animals with slowly produced alloxan diabetes must be made and reported before one can reach a final conclusion that the histologic picture of alloxan diabetes is essentially different from that of the other two experimental forms of the disease. Kennedy and Lukens,[14] as well as Bailey, Bailey and Leech,[10] also noted hydropic degeneration in an animal with alloxan diabetes, but they attributed it to the effect of hyperglycemia on beta cells that had escaped destruction by the alloxan.

In this connection, the experience of Carrasco, described in my last report,[3] is of interest. A dog that he injected with alloxan developed diabetes in a mild form but subsequently recovered. This result makes it clear that the pancreas of an alloxan-injected animal may regenerate just as does the pancreas in diabetes induced surgically or by anterior-pituitary extract. Furthermore, it should be borne in mind that in diabetes in human beings, hydropic degeneration has steadily grown rarer and rarer, with an accompanying decrease in the mortality from the disease in the first days, weeks and months following its onset. It is true that further experiments with alloxan are needed before it can be determined whether the fibrosis and hyalinization of the islands, so frequent in human diabetes, will appear when experimental conditions are set to allow an opportunity for it. Moreover, too little time has been spent by investigators of alloxan diabetes in studying the possibility of altering its course by diet, reduction of blood sugar and the

giving of insulin. Thus, Burn, Lewis and Kelsey[15] demonstrated that rats with alloxan diabetes when placed on a high-fat diet showed a disappearance of the glycosuria, which remained absent until the normal diet had been resumed. An abrupt resumption of the high-fat diet was accompanied by some ketonuria, but on a gradual increase of the fat component the glycosuria disappeared without the development of ketonuria. In other words, alloxan diabetes in rats may at times be controlled by diet. After successive periods of a high-fat diet, the glycosuria seen on a return to a normal diet steadily diminished.

The regular appearance of diabetic cataracts in rabbits, and less frequently in rats, observed by Bailey, Bailey and Leech within two months after injections of alloxan, reminds one of the frequency of such a complication in human beings with diabetes. Such cataracts have been shown in partially depancreatized dogs and also in depancreatectomized rats,[16] and I understand have been reported in the pituitary diabetes of a dog. The observations of the Boston group have been confirmed by Chesler and Tislowitz[17] in rats, and personal communications state that cataracts have been found at various other laboratories, in Cleveland and Philadelphia.

Various birds, such as owls, ducks and chickens, have been intravenously injected with alloxan by Scott, Harris and Chen[18] without developing diabetes. Pigeons, however, developed hyperglycemia and showed normal islets, but with occasional hydropic degeneration. Pigeons, like human beings, do not convert uric acid into allantoin, but they respond to alloxan in the same way as do animals that produce allantoin from uric acid. The same holds true for the Dalmatian hound. Goldner[11] noted the occurrence of a whitish deposit, identified as sodium urate, in the pericardium, pleura and liver of many diabetic pigeons with diabetes. This was not observed by Mirsky[19] in his report of experiments with alloxan in ducks. Hyperglycemia was produced, but as in pigeons, there was only partial necrosis of the islands of Langerhans. Mirsky found necrosis without diabetes when 50 to 750 mg. of alloxan per kilogram of body weight was injected into the wing vein of ducks. Two hundred milligrams caused death within three to forty-eight hours. Hyperglycemia occurred in some birds but not in others. Hypoglycemia was not noted. The islets of ducks appear to be sensitive to large doses of alloxan, but Mirsky states that these birds do not require intact islands to maintain carbohydrate metabolism and thus differ markedly from other species. One duck, following the injection of 50 mg. of alloxan per kilogram, showed necrosis in nine days but no hyperglycemia.

Ramos[20] reports hyperglycemia with sugar values reaching 242 mg. per 100 cc. in turtles two days after the injection of alloxan. Goldner and Gomori[21] pursued their studies on carbohydrate in uric acid metabolism in pigeons following injections of alloxan. The blood sugar was increased from the normal daily level of 150 mg. to 300 to 400 mg. Smaller doses caused a similar syndrome but without a rise in the blood sugar. The uric acid increased from the pre-alloxan level of 4.2 to 7.0 mg. to 8 to 34 mg. in six hours and from 9 to 135 mg. in twenty-four hours. Such an increase has been clinically recognized in human beings as a symptom of visceral gout. It was accompanied by a conspicuous atrophy of the musculature.

The more one experiments with alloxan, the more bizarre are the results. Thus, Thorogood and Zimmermann[22] found that dogs made diabetic with alloxan and subsequently depancreatized required only one third of the insulin needed prior to pancreatectomy. Direct ligation caused little or no drop in the need for insulin. They also found that depancreatized dogs developed acidosis much more easily than did those with alloxan diabetes, although the diabetes in the latter was apparently severer. They thought that there might be a second hormone, possibly residing in the alpha cells, that acted in opposition to insulin and tended to prevent acidosis and coma.

Monkeys develop diabetes and also acidosis following injections of alloxan. This is unusual, as is pointed out by Goldner and Gomori,[21] because monkeys do not always develop severe diabetes following pancreatectomy. According to Orias,[23] rats with 95 per cent of the pancreas removed are more resistant to the diabetic action of alloxan than are normal controls, but with repeated sublimina doses at ten-day intervals they tend to develop diabetes more readily than do normal rats.

Alloxan when introduced into the alimentary tract of rats causes the same changes in the islets of the pancreas, according to Ruben and Yardumian,[24] as those that it produces when injected into the tissues or peritoneal cavity. When this method is employed with a dosage sufficient to produce diabetes, however, distinct hepatic and renal damage occur.

Assays of the pancreases of dogs with alloxan diabetes for insulin show about 0.5 unit per gram, in contrast to the pancreases of normal dogs, which contain 2 or 3 units per gram.[25] For a comprehensive report of the factors affecting the insulin content of the pancreas, one should consult Haist's article.

The hyperglycemia that early results in animals injected with alloxan has been ascribed to gluconeogenesis in the liver. It has been duplicated by the simultaneous injection of adrenalin and insulin into animals. It has been prevented by the injection of alloxan into functionally or anatomically adrenalectomized rabbits, according to Goldner and Gomori.[26] Houssay, Orias and Sara[27] found that hyperglycemia did not occur in hepatectomized dogs or toads. They observed it in adrenalectomized

animals and dogs with a previous section of the splanchnic nerves and in recently hypophysectomized toads.

The hypoglycemia that follows hyperglycemia in animals with alloxan diabetes is not directly caused by alloxan, because it does not occur in depancreatized dogs or dogs already made diabetic with alloxan. Furthermore, the injection of alloxan into eviscerated cats is not followed by a reduction in blood sugar.[28] Hypoglycemia has been thought to be due to the liberation of alloxan from the necrosing degenerated beta cells, and Goldner and Gomori[26] state that whenever hypoglycemia develops, diabetes follows if the animal survives. From this conclusion Houssay et al. dissent. In fact, their conclusions regarding the triphasic blood-sugar changes in animals with alloxan diabetes are as follows:

> (1) The liver is essential for the initial hyperglycemia produced by alloxan. Hyperglycemia is observed in adrenalectomized animals and those with section of the splanchnic nerves. It must be attributed principally to a direct action of alloxan on the liver. (2) The secondary hypoglycemia is not due to liberation of insulin, but to an extrapancreatic effect: probably lack of glucose production by the liver. The liver of the animal already in a diabetic condition is generally insensible to this action of alloxan. (3) The final hyperglycemia is mainly due to the destruction of the beta cells of the islets of Langerhans, and becomes permanent if the animal survives. (4) The liver plays an important role during the three phases of modification of blood sugar level.

Kirschbaum, Wells and Molander[29] conclude as follows from their experiments:

> An initial hyperglycemia did not appear in either adrenalectomized or hypophysectomized rats injected with alloxan. With the doses of alloxan used, hypoglycemic convulsions did not appear in any of 15 intact animals, whereas convulsions occurred within six hours in all of 14 adrenalectomized and in 9 of 10 hypophysectomized animals. In the absence of the adrenal medulla the reaction to alloxan was the same as in intact animals: removal of the adrenal cortex (regenerated cortex following adrenal enucleation) resulted in the same reaction as total adrenalectomy.

Foglia, Orias and Sara[30] injected alloxan subcutaneously into rats and found a prolonged initial hyperglycemia lasting for three to five hours, which was followed by a marked hypoglycemia. In previously pancreatectomized rats, however, subsequent injection of alloxan failed to affect the blood-sugar level.

Thomas and Emerson[31] showed that the pituitary glands of rabbits given intravenously 200 to 300 mg. of alloxan per kilogram of body weight revealed degeneration of the basophils and in some cases areas of necrosis in the adrenal cortex. Rats receiving 400 mg. per kilogram subcutaneously developed similar lesions. Janes and Friedgood[32] demonstrated that rats made diabetic with alloxan showed marked reduction or disappearance of their diabetic symptoms following adrenalectomy. Thus, they respond to adrenalectomy in a manner similar to that shown by pancreatectomized animals.

Pregnant rats injected with alloxan developed diabetes, according to Friedgood and Miller.[33] The alloxan passed through the placenta but did not cause diabetes in the offspring. No reason for this is given. Chesler and Tislowitz[17] found that alloxan dwarfed the growth of immature rats. Lowry and Hegsted,[34] using rats on a thiamin-deficient diet, demonstrated that rats made diabetic with alloxan develop thiamin deficiency at approximately the same rate as normal controls, or perhaps slightly less quickly. Furthermore, the response of the diabetic animals to thiamin therapy was more marked than that of the controls. Schneider, Lewis, Moses and McCullagh[35] report diabetic retinitis associated with reduction of the plasma protein in rabbits made diabetic with alloxan. They describe changes in the lens in 15 rabbits.

With the aid of deuterium, Stetten and Boxer[36] found that on a diet that was 60 per cent carbohydrate one fourth of the urinary glucose formed by rats with alloxan diabetes was synthesized in vivo and the other three fourths was derived from the dietary carbohydrate. The proportion of liver glycogen synthesized from fragments smaller than hexose was greater than had been found in normal rats. Synthesis from fatty acids decreased to 5 per cent of the normal rate. This failure of the diabetic animal to utilize glucose in the synthesis of fatty acids constitutes a major metabolic defect in this disease.

Comparative studies of the action of alloxan on the islet cells of the pancreas and the convoluted tubules of the kidney in the rabbit, the dog and man have been published by Brunschwig and Allen.[37]

Interest in alloxan diabetes continues unabated. Published work in 1945 emanated from at least twenty-five different laboratories in eight countries. With the cessation of the war, one may expect this year twice the number of reports published in 1945.

Carbohydrate Chemistry

Carbohydrate chemistry has made marked strides in the last few years. Perhaps one of the most spectacular discoveries has been the synthesis of glycogen in vitro by Cori.[38] Even more recent is the work of Hastings,[39] who has shown by the use of radioactive tracer elements that a substance seemingly as remote from carbohydrate as bicarbonate of soda can under suitable conditions take part in the creation of a carbohydrate molecule. The influence of insulin on blood pyruvate localized in a general way the action of insulin, but the crucial point in the breakdown of carbohydrate at which there is interference in its utilization, as in diabetes, has always been a mystery. Evidence that may furnish a valuable clue to the solution of the problem has recently been reported by Price, Cori and Colowick.[40] In the utilization of glucose by animal tissues this substance is ordinarily transformed to glycogen by oxidation, which is catalyzed by hexokinase (glucose and adenosine-triphosphate glucose-6 phosphate and adenosine diphosphate). According to these au-

thors, anterior-pituitary extract inhibits this reaction, as shown either by injecting rats with it prior to the preparation of tissue extracts or by adding it to the enzyme preparation in vitro. Moreover, — and this is of vital importance, — this inhibition can be counteracted by insulin, either in vivo or in vitro.

Of particular interest is the statement of Price et al. that rats made diabetic by the injection of alloxan yield tissue extracts that show the same enzyme activity curve as do those obtained from rats made diabetic by anterior-pituitary extract. The brain, they point out, is an apparent exception, since brain extracts prepared from rats injected with alloxan or with anterior-pituitary extract do not show an inhibition of hexokinase activity. Brain extracts can, however, be inactivated by addition of anterior-pituitary extract in vitro.

Anterior-pituitary extract does not inhibit the conversion of glycogen to lactic acid in muscle extract. In a dialyzed liver dispersion, when oxygen consumption is measured, oxidation of glucose is inhibited by anterior-pituitary extract, whereas that of fructose-6-phosphate and of pyruvate is not. Insulin releases hexokinase from inhibition by anterior-pituitary extract in all cases. It does not by itself enhance hexokinase activity under these experimental conditions. Price et al. state:

> Within a certain range the release of inhibition is proportional to the amount of insulin added in vitro. That the in vivo action of insulin is of a similar nature is indicated by the fact that muscle extracts prepared from diabetic rats after the injection of insulin show normal hexokinase activity. When insulin is reduced by cysteine, it no longer exerts its antagonistic effect against anterior-pituitary extract inhibition of hexokinase activity.

The authors promise to discuss in later publications the implications of this important discovery.

Diabetic Neuropathy

An outstanding summary of diabetic neuropathy, with the listing of 171 references, as well as a contribution to the subject, has recently been published by Rundles.[41] Like the reviews by Duff[1] and Haist,[25] elsewhere cited, this work is to be held up as an example for future authors. All these articles deserve detailed comment, but the greater clinical importance of Rundles's paper forces me to give it preference.

Diabetic neuropathy has been described for over fifty years, and such names as Marchal de Calvi, Bouchard, Pavy, Leyden, Charcot and others less familiar have been associated with it. In 1936, Jordan[42] published a comprehensive summary of the data on neuritis available at the George F. Baker Clinic at that time. Rundles's article has been excellently reported in an editorial in the *Journal of the American Medical Association*,[43] to which those who do not have access to the original paper may turn. Several points made by Rundles, based on his experience with 125 cases among somewhat more than 3000 new diabetic patients during a seven-year period, deserve emphasis. Of these he studied 35 personally. From his intensive survey of the literature and his own observations, he reached definite conclusions, which are most important for any physician treating a diabetic patient. He states: "Most diabetics who develop organic disease of the peripheral nerves have had antecedent periods usually of months or years' duration of grossly neglected or poorly managed treatment. There is strong evidence that the disordered metabolism of diabetes mellitus itself is the etiologic factor in this as well as other accompanying diabetic complications." Rundles cites 5 cases of his series in detail. The first of these patients had typical symptoms of neuritis in the fingers and feet, following careless treatment for diabetes. In addition, she had discoloration of the right great toe and a blistered leg, which she attributed to a burn. The toe became dark purple, and pus exuded from it. After four weeks of hospitalization with orthodox treatment of the diabetes by an 1800-calorie diet containing 150 gm. of carbohydrate and 80 gm. of protein, and 10 units of insulin three times a day, the infected toe healed, although there was no definite alteration in the neurologic status.

The second case was that of a boy twenty years old with diabetes of six years' duration. In addition to characteristic symptoms of neuritis in the lower extremities and a so-called "low abdominal bulge," due to a quart of residual urine in the bladder, the patient showed the customary elevated spinal-fluid total protein (69 mg. per 100 cc.), first emphasized by Root.[44] Six weeks after admission, cloudy vision developed. An ophthalmology consultant, finding macular edema, punctate and flame-shaped hemorrhages and extensive areas of exudate, diagnosed severe diabetic retinopathy. Six weeks later there had developed an extensive proliferating retinopathy with both fundi filled with new-formed, dilated and tortuous veins and capillaries, with even more extensive deep and superficial hemorrhages but no further visual impairment. With diabetic control, supplemented by vitamins, the patient was discharged after four months little improved, but was seen at intervals for another eighteen months. The diabetes remained well controlled. He gradually gained in weight and strength, and the retinal hemorrhages became less extensive. To all physicians interested in diabetes the report of the condition of the eyes is significant. The consultant found the retinopathy much improved, reporting only minimal pigmentary disturbance in the regions of former hemorrhage, slight wrinkling and fibrotic scarring in different areas, a few new-formed blood vessels and a rare rosette-shaped hemorrhage. Rundles describes this result as the most astounding recovery of a diabetic retinitis of this type and severity he has ever seen or heard of. Unfortunately, such an experience is unique. Most ophthalmolo-

gists agree that diabetic neuropathy is almost always progressive and that retinitis proliferans rarely, if ever, improves.

The limits of space forbid the citation of the many interesting observations recorded by Rundles, but it must be pointed out that more than one fourth of his patients were less than forty years of age, with 8 of them twenty or younger. There was no predilection for welfare patients as compared with those of average or superior means, but all the patients showed lax diabetic care. No case was seen in which diabetic neuropathy actually preceded the appearance of diabetes mellitus. Furthermore, Rundles states that none of these patients were among those regularly attending his diabetic clinic or under the adequate supervision of competent physicians with provision for enlightened dietary management and checkup visits. These findings confirm the observations of Joslin and Root[45] that the symptoms of diabetic neuropathy always start during a time of uncontrolled diabetes.

Muscular cramps and aching in various parts of the body were early symptoms, and muscular weakness, especially of the legs, was almost uniformly present, 4 of the patients being able to go upstairs at home only by crawling on their hands and knees. Numbness, tingling and paresthesias, and shooting pains, characteristically worse on exposure to cold and at night, making the touch of bedclothes unbearable and sleep impossible, were frequent complaints. The lower extremities were most severely affected. The peroneal nerve was more vulnerable than the tibial, and the ulnar more vulnerable than the radial or median. Occasionally symptoms appeared in the pudendal, femoral or intercostal nerve areas or in asymmetrical areas in the extremities. The Achilles tendon reflexes were absent in 81 per cent of the cases, and patellar reflexes in 56 per cent, and each was diminished in an additional number of cases. Rundles considers diminished or absent tendon reflexes to be the most reliable single sign of diabetic peripheral nerve disease.

Gastrointestinal dysfunction, with diabetic, often nocturnal, diarrhea, and genitourinary and sphincter disturbances, are discussed. Rundles calls special attention to disease of the peripheral autonomic nerves, which was evidenced by damage to the peripheral sympathetic nerves and revealed by sweating, loss of vasomotor and pilomotor control and dependent edema. His knowledge in this regard was gained from the 35 patients whom he studied personally. Among these there were 26 patients who had dependent edema of the lower extremities appearing during the course of the neuropathy, which Rundles ascribed to involvement of the vasomotor nerves. Orthostatic hypotension and orthostatic tachycardia were observed and are also discussed. The association of diabetic neuropathy and retinopathy is emphasized, together with the fact that they may appear in the absence of hypertension, impaired renal function and albuminuria. Wagener, Dry and Wilder[46] pointed out that retinal disease and peripheral-nerve disease were frequently associated in diabetic patients, and that 25 per cent of a large group of patients with diabetic retinitis had diabetic neuritis in addition. Rundles found that the converse relation also held in his patients with diabetic neuropathy, since 43 (34 per cent) of the 125 patients had retinal disease characteristic of that due to diabetes. The coincidence of these two diabetic complications appears to him to be more than fortuitous. Acceptable evidence of occlusive arterial disease in patients with diabetic neuropathy was not unduly frequent. McKittrick and Root[47] have likewise noted the presence of neuritis in a considerable percentage of patients with lesions of the lower extremities in the absence or notable lack of vascular disease.

Deficiencies of vitamins were not observed, and the therapeutic use of vitamins, especially the vitamin B complex, was not found useful. This fact corroborates Jordan's[42] detailed study of 63 patients, in only 1 of whom the diet appeared to have been deficient. Rundles further states that a number of recent patients who had been given no vitamin supplements appeared to be recovering from their neuropathy as rapidly as had any others in the past, and adds that he has never seen clinical improvement in diabetic neuropathy by any treatment regimen in the absence of effective diabetic control.

The diagnosis of diabetic neuropathy is one of the least precise, because it is easy to ignore the muscular weakness, aches and pains of acute diabetic nonregulation, particularly if the neurologic examination is inexpert. All that Rundles writes along these lines emphasizes the importance of an article by the late Dr. Abraham Rudy,[48] in which he reports numerous cases of neuropathy in old-aged diabetic patients who were returned to well-being by the application of prolonged diabetic care and control of their disease.

The prognosis in diabetic neuropathy varies according to the severity of the neuritic disease. Recovery may take place within a few weeks or in six to twelve months, and in severe cases it may require one or two years.

In conclusion, Rundles points out the following:

> Occlusive arterial disease, diabetic cataracts, and advanced stages of diabetic retinopathy are late complications representing irreversible organic changes, which diabetic treatment will not alleviate and for which other treatment offers but poor compensation. Neuropathy, along with early stages of retinopathy and hepatomegaly, should be emphasized as reversible diabetic complications always a warning to both physician and patient of inadequately controlled diabetes which in the course of time, if uncorrected, will lead to widespread and permanent degenerative changes. At least 50 per cent of all diabetics will survive with little or no treatment for many years. In them the ultimate development of degenerative complications is the only criterion by which the adequacy of their treatment can be judged.

This article by Rundles is one of the most important in recent years, since it proves the necessity for painstaking and aggressive treatment of diabetes from its incipiency to its very end.

(To be concluded)

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CAPOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

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CASE 32131

PRESENTATION OF CASE

A sixty-nine-year-old housewife entered the hospital in collapse.

On the morning of admission she had an attack of excruciating substernal and epigastric pain and collapse lasting nearly an hour and followed by a loose bowel movement. Three hours later, in the early afternoon, she was well enough to attempt to stoke the household furnace. While at this task she had a second attack of upper abdominal pain, severer than the first. The pain radiated to the left shoulder. She apparently collapsed and was found lying on the floor about five hours later and was brought to the hospital.

About five years before admission the patient had had an episode of deep right chest pain radiating to the scapula. This attack was said to have been initiated by exercise and relieved by rest. In the following years she had had attacks of epigastric pain approximately every six months; it began as a squeezing, nonradiating pain followed by nausea, vomiting and syncope for one to three hours. There were no intervening symptoms. She had known that she had hypertension for an indefinite number of years. There had been no exertional dyspnea or ankle edema. Many years previously she had had an ovary and a "tumor" removed from the abdomen.

On physical examination the patient was cyanotic and responded poorly. The apical impulse was not visible, and the left border of cardiac dullness was poorly defined, although it appeared to be just outside the midclavicular line. The heart sounds were distant and at times were not heard. There was moderate dullness over the left chest posteriorly from the spine to the posterior axillary line. Breath sounds were diminished over this area. There was severe epigastric tenderness without spasm. No abdominal masses were palpated. There was an old longitudinal midline scar above the symphysis. Rectal examination was negative.

The temperature was 97°F., the pulse 98, and the respirations 25. The blood pressure was unobtainable.

The red-cell count was 4,020,000, with a hemoglobin of 8.5 gm., and the white-cell count 14,100. The urine had a specific gravity of 1.020, and the sediment contained 1 or 2 red cells and 15 to 20 white cells per high-power field. A glove specimen of stool was guaiac negative. The serum amylase was 29 units, and the nonprotein nitrogen 26 mg. per 100 cc. A portable x-ray film of the chest showed poor visualization of the left half of the diaphragm. The heart was enlarged, and there was marked enlargement of the aorta.

On the morning after admission the patient was more alert and her abdominal pain had lessened. She had developed a severe productive cough, and the white-cell count rose to 25,900. There was no change in the temperature or pulse. With plasma and saline the blood pressure rose to 80 systolic, 60 diastolic. At 7:50 p.m. the same day she had a sudden severe pain under the right scapula and in the right axilla. The blood pressure fell slightly but soon rose to 120 systolic, 70 diastolic. At 8:20 p.m. she had another attack of excruciating pain in the same region and suddenly died.

DIFFERENTIAL DIAGNOSIS

DR. ALLAN G. BRAILEY: It seems to me that this woman died of cardiovascular disease. One might think in passing of acute pancreatitis, but when she came to the hospital the serum amylase was found to be normal and the subsequent course seems completely inconsistent with pancreatitis. Pulmonary embolism deserves attention. The pain of embolism, however, is not so agonizing as that described here. Embolism of such degree as to cause collapse would produce marked dyspnea, and there is no mention of evidence of dilatation of the right heart, such as distended neck veins. There is no hint of a likely source of emboli, although the source is frequently obscure. There is no mention of bloody sputum. I do not believe that we need to suppose she had embolism as a primary cause of death.

The two diagnoses that have to be carefully juxtaposed are myocardial infarction and dissecting aneurysm. The story is consistent with infarction. The patient was sixty-nine years old and was therefore likelier to die of coronary disease than of dissecting aneurysm. Five years previously she had had chest pain brought on by effort and which may have been evidence of pre-existing coronary disease. The heart signs and blood pressure are apt to be well maintained in dissecting aneurysm. This patient, however, was obviously in shock when she came in, and the poor quality of the heart sounds and blood pressure could be as logically ascribed to shock as to the underlying condition. The location of the pain was substernal and upper abdominal. Three hours later the second attack was said to have been epigastric. It is a good story for myocardial infarction but pain proceeding downward constitutes one argument in favor of dissecting

aneurysm. There was no pericardial friction rub. Of course that frequently is not present even with massive cardiac infarction. An electrocardiogram would be a great help. Was one taken?

DR. TRACY B. MALLORY: No.

DR. BRAILEY: It seems unlikely that a person three hours after severe infarction would feel like getting up and stoking a furnace.

DR. ROBERT L. BERG: A cardioscope was taken in the Emergency Ward and was negative.

DR. BRAILEY: The fact that she made a temporary recovery to the point where she was willing to stoke the furnace suggests that her attack was due to dissecting aneurysm. She was known to have hypertension for years, a constant prerequisite for dissection. The character of the onset of the pain in these cases is usually significant, but we cannot be too sure what it was like here. If it came on suddenly, it would favor aneurysm. The pain of cardiac infarction comes on over a period of a few minutes. If she had a dissecting aneurysm, the terminal episode of pain in the right chest might have resulted from dissection upward. Four seizures of terrific pain in twenty-four hours favor an aneurysm with discontinuous dissection. It is not likely that she had four such closely repeated infarctions of the heart. Somewhat against dissection is the report that the blood pressure stayed low. If it did stay low, we have to assume that this was due to a state of shock. It may be significant that the last two attacks of pain occurred only after the blood pressure began to rise. A more serious objection is the fact that no evidence is given of occlusion of the branches of the aorta, but some of the intercostal branches might have been occluded without producing obvious symptoms in so sick a patient.

Are there any x-ray films?

DR. MILFORD D. SCHULZ: The film has been lost.

DR. BRAILEY: I should like to know particularly about the aorta. If it was enlarged it might easily have resulted from hypertension and arteriosclerosis. I also wish I knew how big the right ventricle was. Nothing is said about that.

The patient died suddenly. How sudden is "suddenly"? Instantaneous death from heart disease may be due to ventricular fibrillation, to cardiac standstill or to rupture of the heart or aorta, but she certainly had not had coronary occlusion long enough to have ruptured the heart. She could easily have died of a disturbance of rhythm. This is a difficult problem to decide, but I shall vote in favor of dissecting aneurysm and try to justify it on the basis that the pain moved downward, that she had four attacks of terrific pain of sudden onset and that death was instantaneous.

DR. MALLORY: Dr. Berg, will you tell us how the discussion ran on the wards?

DR. BERG: When she first came in she was seen in the Emergency Ward and was in coma. No history was obtainable. She was given intravenous fluids and became somewhat responsive. She had abdominal pain and was extremely tender in the epigastrium. The chief problem was whether her condition represented an intra-abdominal catastrophe or something originating in the cardiovascular system. The surgeons saw her at that time and agreed that there was no immediate need of surgical intervention, and as she improved we were able to get the rest of the story, which focused more closely on the cardiovascular system as time went on. I personally did not see the x-ray film, but Dr. John Stanbury, who admitted the patient, said that it showed a very much enlarged aorta. She was sent up to the wards with a diagnosis of dissecting aneurysm.

So far as the manner of death is concerned, I might add that after the last attack of pain she died within thirty seconds.

DR. CHARLES H. BURNETT: There was no question from the x-ray film that the aorta was markedly enlarged.

DR. MALLORY: Does that alter your opinion, Dr. Brailey?

DR. BRAILEY: No; it rather helps to confirm my diagnosis.

DR. ALBERT J. STUNKARD: The blood pressure, which was unobtainable in the Emergency Ward, was up the next morning.

CLINICAL DIAGNOSES

Dissecting aortic aneurysm.
Arteriosclerotic heart disease.
Bronchopneumonia.

DR. BRAILEY'S DIAGNOSES

Dissecting aneurysm of aorta.

ANATOMICAL DIAGNOSES

Ruptured syphilitic aneurysm of aorta.
Hematoma of mediastinum.

PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient showed a large fusiform aneurysm of the thoracic aorta, not a dissecting aneurysm, but I believe a syphilitic one, despite her advanced age. Patients with syphilitic aneurysm do not ordinarily reach the age of sixty-nine. The specimen grossly was strongly suggestive of syphilis; it showed wrinkling, so-called "tree barking" and stellate scarring of the intima. Microscopically there were many foci of destruction in the media and also a marked perivascular cuffing with lymphocytes and occasional plasma cells, characteristic of syphilitic aortitis. The aneurysm had ruptured, and a massive hematoma of the mediastinum had formed. There was then dissection of this hematoma in various directions — upward to the base of the heart and downward into the serosa of the stomach, a large portion of which was lifted off the muscularis by the clotted blood.

It is quite probable that the epigastric pain and tenderness were directly related to this last extension of blood. It had broken into one pleural cavity, where about 900 cc. of fluid was found, about half of it consisting of blood clots.

It was not a true dissecting aneurysm because, as you know, in a dissecting aneurysm the separation in the aorta is within the media so that muscle fibers of the media are found on each side of the plane of dissection. Under such circumstances the pressure in the newly dissected vessel equals or exceeds that within the main aortic lumen, thus occluding by external pressure the small aortic branches. Dr. Brailey looked for clinical evidence of this phenomenon in the record but could not find it.

CASE 32132

Presentation of Case

A seventy-year-old physician entered the hospital because of persistent vomiting.

Six months before admission the patient began to complain of epigastric fullness and indigestion. He restricted his diet to fluids and soft foods and in six months lost 20 pounds. Ten days prior to admission he had an attack of vomiting, with epigastric discomfort; the vomitus was foul smelling. He was constipated, and enema returns were slight.

On physical examination there was a soft nontender mass in the left upper quadrant that extended from the rib margin to the level of the umbilicus and moved slightly with respiration. There was slight clubbing of the fingers.

The temperature was 98°F., the pulse 90, and the respirations 18. The blood pressure was 140 systolic, 90 diastolic.

The red-cell count was 4,300,000, and the white-cell count 12,200, with 75 per cent neutrophils. The urine had a specific gravity of 1.012; there was no albumin. The prothrombin time was 20 seconds (normal, 14 to 16 seconds), the nonprotein nitrogen 27 mg. per 100 cc., the serum protein 6.1 gm., and the chloride 106 milliequiv. per liter.

An x-ray film of the chest showed bright lung fields. Between unusually prominent pulmonary markings there were dispersed numerous rounded translucent areas. The appearance was consistent with pulmonary fibrosis with some cystic changes. An intravenous pyelogram revealed a tumor mass filling the left flank and kidney area; its outline was indefinite. There was no filling of the left kidney pelvis. The right kidney functioned normally. In a retrograde pyelogram, the left ureter filled throughout. It was small and swung to the right so that it crossed the spine at the fifth lumbar vertebra. The pelvis was flattened, rotated and lay almost to the right of the spine.

A gastrointestinal series taken on the eleventh hospital day showed that the stomach, colon and duodenum were deformed by an apparently extrinsic mass on the left side. The stomach was displaced upward and anteriorly. The duodenal bulb was compressed toward the right. The ligament of Treitz was pressed forward and downward. The descending colon was displaced laterally, and the splenic flexure upward. There was barium in the stomach, terminal ileum and cecum twenty-four hours after the meal.

The patient had a slight fever on the thirteenth day, and there was tenderness in the left costovertebral region. These signs quickly disappeared. Another urine showed 10 to 15 white cells per high-power field, and on culture there was a moderate growth of *Staphylococcus albus*.

An operation was performed on the twenty-second hospital day.

Differential Diagnosis

Dr. Fletcher H. Colby: Since the diagnosis rests largely on the x-ray findings, I shall ask the roentgenologist to interpret the films now.

Dr. James R. Lingley: The chest shows a diffuse linear density throughout both lungs that is consistent with fibrosis. The hilar shadows are prominent and perhaps somewhat nodular. Incidentally, in cases of this type one should always think of diffuse pulmonary metastases. The plain abdominal film shows density throughout the left side of the abdomen, apparently due to a large mass the margins of which are not too well defined. On the retrograde film, there is displacement of the ureters to the right and the kidney pelvis is not well filled. In the intravenous pyelogram there is no evidence of excretion on the affected side. The gastrointestinal films show displacement of the stomach to the right and some displacement of the descending colon.

Dr. Colby: Is the pulmonary picture consistent with metastases?

Dr. Lingley: I think it is more consistent with fibrosis, but metastatic disease is a possibility.

Dr. Colby: The x-ray report states that the renal pelvis on the affected side was flattened and rotated. That is an important finding, but I suggest that the irregularity in this region represents ureter and not renal pelvis.

Dr. Lingley: I believe that you are correct. The pelvis is probably not filled on the affected side.

Dr. Colby: Are these x-ray findings in the gastrointestinal tract — the displacement of the stomach, duodenum and large bowel — quite consistent with a tumor arising from the right kidney?

Dr. Lingley: I believe that the mass is a greatly enlarged left kidney.

Dr. Colby: We have a patient seventy years of age who had had gastrointestinal symptoms for at least six months. He had had persistent vomiting for the ten days before entry. On examination there was found a large mass that filled the left loin and extended down almost to the pelvis on that side. From the x-ray study with pyelograms, intravenous

and retrograde, I think it is fair to say that the mass was definitely localized in the left kidney and was presumably a tumor mass arising from that organ. It is not at all unusual to have gastrointestinal symptoms predominant from renal disease, although they are usually caused by right-sided lesions. These symptoms are regarded as being due either to involvement of the sympathetic nerves that supply the gastrointestinal tract, such as occurs in malignant disease, or to pressure of the enlarged kidney on the adjacent organs. The foul vomitus, the pressure defects on the stomach and duodenum, the displacement of the large bowel and the retention of barium lead one to think that the gastrointestinal symptoms were simply due to pressure from the large left-sided renal mass, particularly since no intrinsic lesion of the gastrointestinal tract was demonstrated.

The essential problem is to determine the nature of the left-sided renal mass. The possibilities to consider are a solid tumor arising from the renal parenchyma, a tumor of the renal pelvis with retention within the kidney, a large solitary cyst of the kidney and hydronephrosis.

So far as a solid tumor is concerned, there are several points that seem to be against it. In the first place, there was lack of bleeding. A single urine examination is recorded, but there were only a few white cells and no red cells. Solid tumors of the kidney, however, can go a long time without either gross or microscopic bleeding. Also against a solid tumor is the fact that the mass was described as being soft. Tumors of the renal parenchyma are firm and hard. The surgeon is frequently uncertain whether a mass involving a kidney is solid or cystic until operation. It seems unlikely, however, that this was a solid tumor. To me the x-ray findings are not characteristic of metastatic disease in the lung.

Tumors of the renal pelvis bleed early and often. This was not the case in this patient.

A solitary cyst of the kidney is a distinct possibility, but we have no definite information that would lead us to believe that this was a solitary cyst. In a solitary cyst there is usually a distinct rounded filling defect of the renal pelvis, which is extremely suggestive and sometimes quite characteristic. We lack that evidence here.

Hydronephrosis seems to be the likeliest cause of this large soft mass. The patient had had no pain, but this can be explained by the slow development of the hydronephrosis. There had been no pain suggestive of calculus, and there is no shadow of stone by x-ray. There is, of course, a possibility of a nonopaque stone, but the fact that the patient had had no attacks of pain in the past is somewhat against this. The most probable cause of the hydronephrosis seems to be obstruction at the ureteropelvic junction, although the actual lesion is frequently not demonstrable at the time of operation.

DR. TRACY B. MALLORY: Are there any suggestions or questions?

DR. W. WILSON SCHIER: Could a retroperitoneal lipoma fit this picture?

DR. COLBY: I have had little experience with retroperitoneal lipomas.

DR. MALLORY: Dr. Smith, will you tell us about your operative findings?

DR. GEORGE G. SMITH: This patient had a large hydronephrosis, which extended well across the midline and seemed to push directly against the lower part of the stomach. There was nothing particularly remarkable about it. I do not remember whether the obstruction was at the ureteropelvic junction.

DR. MALLORY: The operative note mentions a double pedicle. Would that suggest that aberrant vessels might have been the cause of the hydronephrosis?

DR. SMITH: It might, but I do not know.

CLINICAL DIAGNOSIS

Cyst of left kidney.

DR. COLBY'S DIAGNOSIS

Hydronephrosis: left kidney.

ANATOMICAL DIAGNOSIS

Hydronephrosis: left kidney.

PATHOLOGICAL DISCUSSION

DR. MALLORY: What this hydronephrosis had to do with the patient's major symptoms, which were gastrointestinal, remains a problem. From the postoperative record it is evident that he was not relieved of the gastrointestinal symptoms by the removal of the kidney. Repeated x-ray examinations showed persistent gastric stasis, and eventually the stomach was explored by Dr. L. S. McKittrick. He was unable to find any organic obstruction but nevertheless did a pyloroplasty, with some degree of relief.

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MERGER AND MEDICAL SERVICE

There has been considerable interest and excitement in recent months about the proposed merger of the armed forces in this country. The obvious advantages from the point of view of efficiency and the importance of co-ordinated effort by all branches of the armed forces in modern warfare have been widely discussed. The resistance to such a merger by those who suspect that their branch might become subordinated in the course of such a merger is, of course, understandable. Nevertheless, the Secretary of the Navy has recently announced that plans are being drawn up and action is already being taken for the merging of several types of facilities that are now duplicated in the Army and Navy. This is the first departure during peacetime from the traditional and not always good-natured rivalry between the different branches of the service. Arrangements are already being made for merging or co-ordinating activities of Army and Navy facilities in matters concerning procurement, intelligence, ports and shipping, air transport services and even recruiting and training.

No specific mention was made in this announcement about the merging of the medical departments of the services, but that is obviously an important function that could easily benefit by some sort of co-ordination and, probably better still, by complete unification. Although it may sound quite radical, it might not even be amiss to consider the possibility of removing the medical services entirely from the armed forces during peacetime, running them in conjunction with existing civilian institutions.

A good deal has appeared both in the medical and in the lay press about the superior quality of the medical services that were rendered to the armed forces during the war. The low case-fatality rates and the improved cure rates, as compared with those obtained in similar conditions during the last war, are always quoted as proof of this contention. Much of this improvement in end results, however, can readily be ascribed to technics and to life-saving therapeutic measures that had been evolved after the end of World War I but before the beginning of this war. In spite of this, there are still discrepancies between civilian and military practice that leave much to be desired.

One naturally expects the medical services of the armed forces to provide the best and most modern forms of treatment and care. Whether the actual accomplishments during this war are uniformly of as high a quality as one has been led to believe is open to question. Obviously open criticism of the services by officers while they are on active duty is well nigh impossible. In private, however, many of them have been quite vocal in their condemnation of many features of these services. It is to be hoped that, now that the war is over, their criticisms can be aired, and that the causes of any justifiable complaints can be ferreted out and corrected. Many physicians of high professional caliber have seen active service in all branches of the armed forces.

Some of them were fortunate, having had the opportunity to utilize their skills to the fullest. Others of equal attainment spent most of their time in "paper work," while holding rather exalted ranks, and still others were treated much as enlisted men, being ordered to do menial duties without any reference to their skills and training. When these officers return to a civilian status, they may prefer to forget their gripes and to get back to their jobs, but they can render an important service by presenting and analyzing their observations and criticisms, unhampered by service regulations.

There are undoubtedly many features of medical service that could be improved as a result of the merging of the medical branches of the armed forces. A uniform and, it is hoped, better policy concerning appointments and assignments to duties based on experience and skill could well be instituted. The services and advice of leading medical authorities could then be better utilized than they have been in the past. A co-ordination of hospital and other facilities for the best management of all types of medical problems, as well as for research, would also accrue to the benefit of all the services. In setting up a new medical department, provision could be made for co-ordinating its activities with those of established medical centers, particularly, although not exclusively, those connected with teaching hospitals and medical schools, much in the same manner as is now being contemplated for the Veterans Administration. Inspiration derived from medical teachers, from those actively engaged in research and perhaps even from collaboration in research activities would help maintain the morale of the medical officers who elect to remain in service.

ALBRECHT VON HALLER — PHYSICIAN-EXTRAORDINARY

Albrecht von Haller was born at Berne, Switzerland, on October 16, 1708. It is reported that when he was ten years of age he could speak Latin, Greek, Hebrew and Chaldaic, having written ve ses in Latin, dictionaries for the Greek and Hebrew and a grammar for Chaldee. He studied medicine at Tübingen under Cavernarius and then at Leyden under Boerhaave and Albinus, receiving his medical degree at nineteen, after submitting a thesis that proved that the so-called "salivary duct" claimed as a discovery by Coschwitz was a simple blood vessel.

He traveled for two years, visiting the University of Paris and the University of London, and then returned to Switzerland to study botany at Basle. He began a collection of plants that became the basis of his tremendous work on plant classification and Swiss flora published in 1742. In his spare time he wrote stories and verses. One of his poems, "*Die Alpen*," is still found in the anthologies.

Von Haller then returned to Berne, where for seven years he engaged in general practice. He applied for the post of city physician but was rejected with the comment: "He is a poet. Why should he want to be a hospital physician?"

At the age of twenty-eight, his growing fame as a botanist and an anatomist led to his appointment by George II to the chair in botany, anatomy, surgery and medicine at the newly founded University of Göttingen, and during the next seventeen years he demonstrated a productivity of scientific research and study that has probably never been equaled. He lectured on the subjects covered in his appointment and in addition wrote a history of medicine, the first textbook of physiology, an atlas of angiology, one on pathology and the volume on the classification of plants previously mentioned. In original research he proved that muscle irritability was independent of nerve supply; that bile was concerned with fat digestion; that the pleural cavities contained no air; and that the heart beat was automatic in origin. He described the development of the embryo and the anatomy of the organs of generation and of the brain. In addition, he accurately explained the mechanism of respiration.

Von Haller founded the *Göttingische gelehrte Anzeigen*, a monthly journal, to which he contributed the almost unbelievable total of twelve thousand papers on almost every branch of knowledge. He continued to write verse and published several historical novels. It is difficult to envisage the circumstances under which this work was done, since it should be remembered that the time was the early

eighteenth century, thirty years before the Revolutionary War.

In 1753, at the age of forty-five, he returned to Berne, where in the next twenty-five years he occupied several municipal and state offices. He prepared his *Bibliotheca medica*, of which he completed the botanical, anatomical, surgical and medical portions, a work that fills ten quarto volumes. He rewrote his elements of physiology in four quarto volumes. He continued his nonmedical writing and published a history of Alfred the Great and two other philosophical romances, *Usong* (1771) and *Fabius und Cato* (1774). He continued his classical studies by writing commentaries on Greek and Latin texts. With all this, until his death in 1777, he found time and energy to carry on a voluminous correspondence with the great scientists of his day.

Although the most famous surgeon of his time he would not operate on human beings. So great was his fame that some pirates who captured an English ship and found on it a package of books directed to him, considered it a crime to rob so learned a man and hurried to the nearest port in order that the books might reach him as soon as possible.

Von Haller was undoubtedly one of the most extraordinary men to grace the profession of medicine, yet he receives scant recognition in modern medical textbooks. Many anatomies do not associate his name with one of his important discoveries, —the vas aberrans, — and the majority of textbooks on physiology do not refer to him at all.

MASSACHUSETTS MEDICAL SOCIETY

SPECIAL MEETING OF THE COUNCIL

A special meeting of the Council of the Massachusetts Medical Society will be held in Boston on Wednesday, April 10, 1946, at 10:30 a.m., in Building E, Harvard Medical School, Longwood Avenue.

Business:

1. Report of the Committee Appointed to Confer With Major General Hawley, Medical Administrator of the Veterans Administration, concerning the medical care of veterans by civilian physicians.
2. Schedule to cover fees for services under this heading.

MICHAEL A. TIGHE, M.D., *Secretary*

Building E is the first building on the right when the quadrangle of the Medical School is entered from Longwood Avenue.
Councilors are asked to sign one of the attendance books before the meeting. The Cotting luncheon will be served at 1:00 p.m. in the Dining Room of Vanderbilt Hall.

SECRETARY'S OFFICE

SURPLUS PROPERTY FOR VETERAN MEDICAL OFFICERS

Few discharged medical officers appreciate the fact that they are entitled to a priority in the purchase of surplus medical equipment, when, as and if it is available, and the majority of those who are aware of this fact have no idea concerning what steps to take in purchasing such equipment.

All who intend to apply must first obtain certification from one of the district offices of the War Assets Corporation. Four such offices are located in Massachusetts, as follows:

Boston
Henry Boltz, district manager
1 Court Street
Tel.: LAFayette 7500

Lowell
E. J. Moriarty, acting district manager
8 Merrimack Street
Tel.: Lowell 6388

Springfield
Lee Manley, district manager
1200 Main Street
Tel.: Springfield 3-7857

Worcester
G. W. Grebenstein, district manager
340 Main Street
Tel.: Worcester 6-4391

At such an office, on presentation of his orders for separation under honorable conditions and his certification that the equipment is for use in his own professional enterprise, the veteran's application for the described property is approved on Form 66. He retains one copy, for use at the time of inspection or purchase of what he desires, and the other copy is forwarded to the appropriate disposal agency, which in the case of New England purchasers of medical equipment is the Consumer Goods Division, War Assets Corporation, 600 Washington Street, Boston. When this disposal station has acquired enough material to make a sale worth while, those veterans interested in the type of goods to be sold will be sent a catalogue, giving the stock number, Army nomenclature and price of the material offered and place where it may be inspected prior to the sale.

The veteran may be present in person at the sale or he may write to the disposal agency, giving his case number (from Form 66), applying for whatever articles he desires to purchase and enclosing a certified check. An opportunity to inspect the various items that are offered for sale may or may not be given, depending on the location of the stock. The sale to veterans will extend over a period of about two weeks on each lot offered.

To avoid disappointment, veterans should realize that they do not have the first choice on these goods. The first priority goes to federal agencies, and the second priority to agencies of a state, county or municipality. After these purchasers have been satisfied, the veteran has his chance, and what is then left is offered to nonprofit institutions, such as hospitals, and finally to the public. There is a movement on foot in the Congress to move the veteran doctor from the third priority class to the second.

MICHAEL A. TIGHE, M.D., *Secretary*

REVIEW LECTURE COURSE

Two changes have been made in the program of the Postgraduate Review Lecture Course recently forwarded to all registered physicians in Massachusetts.

In the first place, the time of the meeting on Wednesday, May 8, has been changed, the four speakers beginning their talks at 3:00, 3:45, 4:30 and 5:15, respectively.

Secondly, the title of the exercise on Monday, May 13, has been changed from "Round-Table Discussion on Obstetrics in General Practice" to "A Critical Review of Progress in Obstetrics during the Last Four Years, including a Consideration of Certain Immediate Problems of the Newborn."

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR FEBRUARY, 1946

RÉSUMÉ

Diseases	February 1946	February 1945	Seven-Year Median
Anterior poliomyelitis	1	3	0
Chancroid	1	1	*
Chicken pox	764	1340	1347
Diphtheria	21	14	12
Dog bite	503	497	531
Dysentery, bacillary	9	9	12
German measles	216	116	116
Gonorrhea	494	303	303
Granuloma inguinale	0	0	*
Lymphogranuloma venereum	1	3	*
Malaria	102	53	1
Measles	1141	305	1876
Meningitis, meningococcal	21	21	12
Meningitis, Pfeiffer-bacillus	2	3	2
Meningitis, pneumococcal	4	2	4†
Meningitis, staphylococcal	0	0	0†
Meningitis, streptococcal	0	0	0†
Meningitis, other forms	0	0	0†
Meningitis, undetermined	3	6	6†
Mumps	639	1888	1091
Pneumonia, lobar	224	241	461
Salmonella infections	8	4	3
Scarlet fever	707	1201	1201
Syphilis	526	351	363
Tuberculosis, pulmonary	218	192	179
Tuberculosis, other forms	11	14	14
Typhoid fever	1	2	3
Undulant fever	0	1	2
Whooping cough	411	595	658

*Made reportable December, 1943.
†Four-year average.

COMMENT

Measles, this month, showed a fourfold increase over last year's near record low. Mumps reached its lowest February figure in 10 years. Chicken pox was at its lowest since 1929.

Record low figures were reported for lobar pneumonia and tuberculosis, other forms.

The first cases of typhoid and anterior poliomyelitis for the current year were reported during February.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Stoughton, 1; total, 1.

Diphtheria was reported from: Arlington, 1; Boston, 7; Camp Edwards, 1; Gloucester, 2; Haverhill, 1; Lynn, 1; Malden, 1; Somerville, 2; Southampton, 1; Springfield, 1; Taunton, 2; Wellfleet, 1; total, 21.

Dysentery, amebic, was reported from: Cambridge, 1; Revere, 1; Waltham (Regional Hospital), 1; total, 3.

Dysentery, bacillary, was reported from: Marblehead, 3; Wrentham (State School,) 6; total, 9.

Hookworm was reported from: Camp Edwards, 1; total, 1.

Malaria was reported from: Athol, 1; Bedford, 1; Belmont, 1; Beverly, 1; Boston, 17; Braintree, 1; Brockton, 1; Brookline, 1; Cambridge, 2; Camp Edwards, 7; Chelsea, 1; Dedham, 1; Everett, 2; Franklin, 1; Gardner, 2; Haverhill, 1; Holbrook, 3; Leicester, 1; Leominster, 1; Lynn, 2; Lynnfield, 1; Malden, 3; Marblehead, 1; Marlboro, 2; Medford, 1; Melrose, 1; Methuen, 1; Milton, 1; Norwood, 2; Peabody, 4; Quincy, 2; Revere, 1; Rowley, 1; Salem, 1; Saugus, 1; Somerset, 1; Somerville, 3; Springfield, 2; Taunton, 2; Tyngsboro, 1; Wakefield, 1; Walpole, 1; Waltham, 2; Waltham Regional Hospital, 10; Wellesley, 1; Wilmington, 1; Worcester, 6; total, 102.

Meningitis, meningococcal, was reported from: Boston, 4; Braintree, 1; Cambridge, 1; Everett, 1; Fall River, 3; Framingham, 1; Gloucester, 1; Leominster, 1; Lexington, 1; Milford, 1; Newton, 1; Southbridge, 1; Taunton, 1; Waltham, 1; Waltham Regional Hospital, 1; Worcester, 1; total, 21.

Meningitis, Pfeiffer-bacillus, was reported from: Falmouth, 1; New Bedford, 1; total, 2.

Meningitis, pneumococcal, was reported from: Boston, 1; Cambridge, 1; Everett, 1; Framingham, 1; total, 4.

Meningitis, undetermined, was reported from: Cambridge, 1; Westfield, 2; total, 3.

Salmonella infections were reported from: Brockton, 1; Cambridge, 4; Fitchburg, 1; Holyoke, 1; Norwood, 1; total, 8.

Septic sore throat was reported from: Barre, 1; Boston, 7; Haverhill, 2; Merrimac, 2; North Adams, 1; Salem, 1; total, 14.

Tetanus was reported from: Fall River, 1; total, 1.

Trichinosis was reported from: Danvers, 1; Somerville, 1; Westport, 2; total, 4.

Typhoid fever was reported from: Malden, 1; total, 1.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

Clinic	Date	Clinic Consultant
Salem	April 1	Paul W. Hugenberger
Haverhill	April 3	William T. Green
Lowell	April 5	Albert H. Brewster
Brockton	April 11	George W. Van Gorder
Pittsfield	April 15	Frank A. Slowick
Springfield	April 16	Garry deN. Hough, Jr.
Fall River	April 22	David S. Grice
Hyannis	April 23	Paul L. Norton
Worcester	April 26*	John W. O'Meara

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments.

*Day changed.

CORRESPONDENCE

A PLEA FOR THE GENERAL PRACTITIONER

To the Editor: Looking back over more than twenty-five years of general practice, with all their rough spots, as well as their smooth and pleasant ones, I feel grieved that the term "general practitioner," with its broad but plebeian meaning, has had no chance to lift itself from its lowly stratum in the medical world. How often the phrase, "He is a great specialist." Has anyone ever heard, by chance, a remark such as, "It is remarkable how many things Dr. —— can do, and do well"? It is certainly seldom uttered by a fellow physician, and a layman never makes the remark with the same sure confidence with which he tells the world: "Dr. —— is going to operate on my wife. He is a fellow of the American College of Surgeons." Hence my thesis, Why not an American College of General Practitioners?

What percentage of medical men are general practitioners? I certainly believe that they compose the majority. The economic exigencies of rural medicine make this statement sure. Throughout the history of medicine, it has been commonly recognized that general practitioners form the largest and most important subdivision of medical practice.

It is also true, that this group has furnished many men who have become outstanding in the medical world. We are indebted to the general practitioner for many of the outstanding advances in our science, and even if this were not so, the general practitioner is still in a position to evaluate the patient's complaints and physical findings and either treat the patient or intelligently refer him to one who can treat him better.

In my mind, the movement toward the narrower specialties may be directly traced to the fact that the general prac-

titioner has never been accorded his just professional recognition. To quote from an article by Dr. Russell L. Cecil in the May, 1945, issue of the *Medical Clinics of North America*: "... during the last five decades a great variety of new specialties have appeared in the field, and many internists are devoting almost their entire time to such subjects as tuberculosis, diabetes, arthritis, allergic diseases and disorders of the endocrines. Personally, I believe this is a wholesome trend. However, it is very important for these highly specialized practitioners to maintain their contacts with the whole field of internal medicine. Otherwise, they become so narrow in their point of view that their approach to all medical problems is completely dwarfed. . . . The rapid development of these subspecialties makes it difficult at times for the general practitioner to discover just what constitutes his domain today in the field of practice. Perhaps the establishment of group clinics will lead to a solution of these confused borderlines."

With a deep sense of respect and appreciation for all that Dr. Cecil stands for in the world of medicine, I cannot but feel that this statement tends to put the general practitioner more or less out on a limb. In spite of this, he warns these highly specialized practitioners, the specialists, to keep close to general practice lest they become narrow.

What have our medical societies done for this large cooperative and all too submissive majority of medical men called general practitioners except to accept their support to further the exclusiveness of and to create more fellowships and boards for the minority specialists?

For the purpose of furthering the cause or elevating the status of the general practitioner, to me it seems needless to discuss his comparative mental equipment. Does it not require as much training, ability and experience to do well almost everything pertaining to the care of the sick as it does to do expertly just one division of this whole? It may be the opinion of many of our specialists that the general practitioner of tomorrow will be a kind of trained greeter or steerer whose chief function will be to find the groove in which his patient is put to get to the proper specialist. Contrary to this thought, numerous writings appear from time to time in reference to the lot of the general practitioner. Dr. James L. Halliday in the June, 1943, issue of the *British Journal of Medical Psychology* expressed the following opinion: "Members of our profession are becoming increasingly separated in function and the medical outlook of each is tending to be constricted to some partial or special view. As a result, there is a tendency to ignore the underlying system of medical thought which unifies our diverse observations and activates and enables us to place them in a proper setting and perspective." In this same article, Dr. Halliday further states, "In the future of organized medicine, the general practitioner who has received a training in human biology will be pivotal in importance, and specialists will be regarded merely as his technical assistants."

Here and elsewhere, Dr. Halliday has ably pointed out the fallacies into which a mechanistic concept of disease must lead. Sound etiology will force us to accept old Cicero's dictum, *Nihil humani alienum a me puto*, which, freely translated, means "There isn't a thing about my patient that I may not need to know." No system of medical records, no matter how skillfully contrived, can dispense with the integrating intelligence of a trained, experienced mind. Here the sum of the parts is less than the whole. This integrating intelligence must stand near the beginning of the therapeutic process. There have been rhapsodies about the good old-fashioned family doctor. They are not all empty praise, although no doubt that good old fellow in the horse and buggy was paid half in cash and half in love, which was not the right formula. But we all know that the accomplishments of medical practice are not to be explained in engineering terms.

Now that I am no longer a general practitioner but have confined my work to internal medicine, I believe that it is not presumptuous of me to thus plead for recognition of the general practitioner. At the present time, any man who limits himself to a specialty, has, if qualified, an opportunity to pass the examination of a board and to become recognized by his fellows in his special field of work. This is true not only of the highly developed specialties, such as eye and x-ray, but also of the more comprehensive specialties, such as surgery and internal medicine. Why should not a well qualified general practitioner have the opportunity to pass a board examination in his general field that would put him on equal footing with his brethren who have qualified in more limited fields?

With these thoughts in mind, why is it not feasible to establish the Board of General Practice or the American College of General Practitioners, or whatever it may be called, which would offer the same inducement to study and improvement that is accorded to men in other recognized specialties?

Those who have devoted years of study to the details of qualifications in the specialties would be abler than I to specify eligibility regarding training, hospital experience, practical experience and the amount, if any, of formal postgraduate instruction.

I am cognizant of the fact that the difficulties of setting up proper standards in such an inclusive specialty would be greater than those that have been experienced in the more limited fields. I am sure, however, this is not an unsurmountable barrier. Certainly it is worth the attempt, and such action would be a potent factor in raising the standards of and making more attractive the practice of general medicine.

Should my hopes and pleadings bear fruit, I am sure that the family physician, an American institution with more tradition and sentiment than any other branch of American medicine, will find a new life incentive and goal to work for and that this will bring righteous recognition from his fellows. His will be a chance, similar to that of his confreres in the specialties, for appreciation and recognition by the millions whom he serves day and night, regardless of the physical or mental troubles with which they may be afflicted.

Fred C. Atkinson, M.D.

257 Main Street
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BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

The Examination of Reflexes: A simplification. By Robert Wartenberg, M.D. With a foreword by Foster Kennedy, M.D. 12°, cloth, 222 pp., with 7 illustrations. Chicago: The Year Book Publishers, Incorporated, 1945. $2.50.

The author in this short manual has attempted to classify and unify the reflexes. Each reflex and the methods for testing and evaluation are discussed in a separate section. The important literature on the subject has been reviewed and noted in the text. A bibliography of 465 references is appended.

The Management of Obstetric Difficulties. By Paul Titus, M.D., obstetrician and gynecologist, St. Margaret Memorial Hospital, Pittsburgh, and consulting obstetrician and gynecologist, Pittsburgh City Homes and Hospital, Mayview and Homestead Hospital, Homestead, Pennsylvania. Third edition. 8°, cloth, 1000 pp., with 426 illustrations and 8 color plates. St. Louis: C. V. Mosby Company, 1945. $10.00.

The first edition of this authoritative reference work was published in 1937, and the second in 1940; this third edition has been extensively revised to bring it up to date and incorporate the new material of the past five years. Additions and changes have been made in the chapters on sterility, ante-partum care, the general management of pregnancy, labor and the puerperium and their complications. X-ray pelvimetry has been rewritten and simplified, and the chapters on toxemia in pregnancy have been thoroughly revised, with the addition of a proposed new classification of toxemias. The chapter on intravenous infusions and blood transfusions has been completely revised, and the related subjects of Rh incompatibilities and erythroblastosis brought up to date. Caudal analgesia has been added to the chapter on anesthesia. The technics of extraperitoneal cesarean section are described, with a number of detailed new illustrations. The use of penicillin in puerperal sepsis, gonorrhea and syphilis complicating pregnancy, and in pyelitis and other infections, as well as the dosage and technic of administration, are discussed in considerable detail. This book should be in the reference libraries of obstetricians and all physicians practicing obstetrics, as well as medical libraries, especially those of hospitals.

Courage and Devotion Beyond the Call of Duty: Being a partial record of official citations to medical officers in the United States Armed Forces during World War II. Preliminary edition. 16°, paper, 254 pp. Evansville, Indiana: Mead Johnson and Company, 1944.

In this preliminary edition, short sketches are provided of various physicians who have received military and naval awards for courageous action in combat or for outstanding achievement in medical service. Short biographies are listed alphabetically, and each describes briefly the action for which the citation or award was made. This small book is unusual and a worth-while addition to the medical history of World War II.

Estudos Cirúrgicos. Vol. 4. Eurico Branco Ribeiro, director of Sanatorio Sao Lucas. 8°, cloth, 280 pp., illustrated. Sao Paulo, Brazil: Libraria Atheneu, José Bernades, 1945.

In this volume Dr. Ribeiro has continued his collection of clinical cases covering the whole field of surgery. A number of the interesting cases are documented with selected lists of references to the medical literature. A combined index for the four volumes of studies has been appended to the text, making available all the cases in the four series, the first of which was published in 1934.

Penicillin Therapy, including Tyrothricin and Other Antibiotic Therapy. By John A. Kolmer, M.S., M.D., Dr. P.H., Sc.D., LL.D., L.H.D., professor of medicine, School of Medicine and School of Dentistry, Temple University, and director of the Research Institute of Cutaneous Medicine. 8°, cloth, 302 pp., with 22 illustrations and 20 tables. New York: D. Appleton–Century Company, Incorporated, 1945. $5.00.

This small book has been written for the medical and dental professions and is largely based on the literature for 1944 and 1945. Various methods of administration are fully discussed. Necessary laboratory procedures are included.

NOTICES

ANNOUNCEMENTS

Dr. R. Cannon Eley has returned from naval duty and will resume the practice of pediatrics at the Children's Hospital, 300 Longwood Avenue, Boston.

Dr. Benjamin Cohen announces his return from military service and the opening of an office for the practice of psychiatry and neurology at 520 Beacon Street, Boston.

Dr. James M. Faulkner, having returned from military service, is resuming the practice of internal medicine at 262 Beacon Street, Boston.

Dr. Calvin B. Faunce announces his return to the practice of otolaryngology at 290 Commonwealth Avenue, Boston.

Dr. Joseph Hahn, on termination of his military service, announces the reopening of his office at 121 Chestnut Street, Springfield.

Dr. Samuel Levine, having returned from military service, announces the opening of an office at 40 Baltimore Street, Lynn, for the practice of orthopedic surgery.

Dr. Henry M. Pollock, Jr., announces his separation from military service and the opening of offices for the practice of urology at 549 High Street, Westwood, and 536 Commonwealth Avenue, Boston.

Dr. N. S. Scarcello announces that he has been released from active duty with the United States Navy and will resume the practice of urology at 11 Irving Street, Worcester.

Dr. D. Thomas Staffier announces the removal of his offi to 21 Breed Street, East Boston.

Dr. Jonathan Zonis announces the removal of his office fro 300 Seaver Street, Roxbury, to 371 Commonwealth Avenue Boston.

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will b held in the auditorium of the Beth Israel Hospital on Tuesda April 9, at 8:15 p.m. Dr. Alvan L. Barach will speak on th subject "Treatment of Chronic Pulmonary and Sinus I fections." A discussion by Dr. Maurice S. Segal and D Daniel Miller will follow.

NEW ENGLAND DERMATOLOGICAL SOCIETY

The regular annual meeting of the New England Der matological Society will be held in the Skin Out-Patien Department of the Boston City Hospital on Wednesday April 10, at 2:00 p.m.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9-10 a.m.

MEDICAL CONFERENCE PROGRAM

Wednesday, April 3 — Cerebral Hemorrhage. Dr. R. D Adams.
Friday, April 5 — Experiences with the Use of Universa Donor Blood and Pooled Plasma Transfusions. Dr C. P. Emerson.
Wednesday, April 10 — Medical Experiences in the Navy Dr. R. P. McCombs.
Friday, April 12 — The Roentgenological Changes in the Gastrointestinal Tract in Scleroderma. Dr. R. Schatzki
Wednesday, April 17 — The Diagnosis of Ruptured Mem branes by the Vaginal Smear. Dr. G. A. Bourgeois.
Friday, April 19 — Holiday.
Wednesday, April 24 — Atrophies, Hypertrophies, and Neoplasms of the Skin. Dr. F. M. Thurmon.
Friday, April 26 — Vagus Resection in the Management of Peptic Ulcer. Dr. F. D. Moore.

On Tuesday and Thursday mornings, Dr. S. J. Thann hauser will give medical clinics on hospital cases. On Saturday mornings, clinics will be given by Dr. William Dameshek. Medical rounds are conducted by some of the staff members from 12:00 to 1:00 in the Lecture Hall.

All exercises are open to the medical profession.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The general oral and pathological examinations (Part II) for all candidates will be conducted at Chicago, by the entire Board from Monday, May 6, through Saturday, May 11, 1946. The Palmer House in Chicago will be the headquarters for the Board. Formal notice of the exact time of each candidate's examination will be sent to him several weeks in advance of the examination dates. Hotel reservations may be made by writing direct to the Palmer House.

Candidates for re-examination in Part II must make written application to the secretary's office not later than April 15

Candidates in military or naval service are requested to keep the secretary's office informed of any change of address.

Deferment without time penalty, under a waiver of the published regulations applying to civilian candidates, will be granted if a candidate in service finds it impossible to proceed with the examinations of the Board. Applications are now being received for the 1947 examinations. For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh, 6.

(*Notices continued on page xix*)